UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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LAURA ALLEN, INDIVIDUALLY; And As ADMINISTRATRIX OF THE ESTATE OF DANIEL ALLEN; And As NEXT FRIEND OF TAYLOR ALLEN AND DANIELLE ALLEN; And MARK ALLEN,

Plaintiffs

vs. No. 05-40048-FDS

MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES; SOUTHWEST RECREATIONAL INDUSTRIES, INC., d/b/a MARTIN SURFACING,

Defendants

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DEFENDANTS' DAUBERT MOTION FOR SUMMARY JUDGMENT and/or TO PRECLUDE PLAINTIFF'S EXPERT TESTIMONY OF DR. MARCIA RATNER

Now comes the Defendant, Southwest Recreational Industries, Inc. (hereinafter "Defendant") and hereby moves this Honorable Court to grant summary judgment in its favor and to preclude the Plaintiff from introducing the opinion of expert witness Dr. Marcia Ratner. As reasons wherefore, the Defendant states the follows and incorporates the arguments set forth in Defendants' Daubert Motion for Summary Judgment and/or to Preclude Plaintiff's Expert Testimony of Dr. Marcia Ratner:

CONCISE STATEMENT OF MATERIAL FACTS GENERALLY NOT IN DISPUTE VIEWED IN THE LIGHT MOST FAVORABLE TO THE PLAINTIFF PURSUANT TO LR 56.1

I. Introduction

This is a toxic tort case. It arises from a wrongful death claim, pursuant to M.G.L. c.229 §2. See attached Plaintiff's Third Amended Complaint, "Exhibit A", hereinafter "Complaint" The Plaintiff, Laura Allen, asserts that the death of her late husband, Daniel Allen, was hastened by the negligent and/or grossly negligent application of the gymnasium floor by the Defendant, in the field house at the College of the Holy Cross in late May early June 2001. Complaint. The plaintiffs make thirteen (13) claims against the Defendants as follows: General Negligence; Negligent Failure to Warn; Loss of Consortium and for Other Relief Available under G.L. c. 229; Conscious Pain and Suffering; Wrongful Death Caused by Grossly Negligent Conduct; Violation of M.G.L. c.93A; Wrongful Conduct; Strict Liability; Breach of Express Warranty; Breach of Implied Warranty; Negligent Infliction of Emotional Distress; Intentional Infliction of Emotional Distress; and Defective Design, Manufacturing and Distribution. Complaint.

Mr. Allen was diagnosed with ALS in January 2002 by Drs. Chad and Russell. See Rule 26 Opinion of Dr. Christine Oliver 9, attached as "Exhibit B", hereinafter "Oliver Opinion".

The National Institute of Neurological Disorders and Stroke define ALS as follows:

> Amyotrophic lateral sclerosis (ALS), sometimes called Lou Gehrig's disease, is a rapidly progressive, invariably fatal neurological disease that attacks the nerve cells *(neurons)* responsible for controlling voluntary muscles. In ALS, both the upper motor neurons and the lower motor neurons degenerate or die, ceasing to send messages to muscles. Unable to function, the muscles gradually weaken, waste away, and twitch. Eventually the ability of the brain to start and control voluntary movement is lost. Individuals with ALS lose their strength and the ability to move their arms, legs, and body. When muscles in the diaphragm and chest wall fail, individuals lose the ability to breathe without ventilatory support. The disease does not affect a person's ability to see, smell, taste, hear, or recognize touch, and it does not usually impair a person's thinking or other cognitive abilities. However, several recent studies suggest that a small percentage of patients may experience problems with memory or decision-making, and there is growing evidence that some may even develop a form of

dementia. **The cause of ALS is not known, and scientists do not yet know why ALS strikes some people and not others.** (emphasis supplied) http://www.ninds.nih.gov/disorders/amyotrophiclateralsclerosis/amyotrophiclateralsclerosis.htm; see also Rule 26 Opinion of Dr. Marcia Ratner 8-9, attached as "Exhibit D", hereinafter "Ratner Opinion".

Experts for both the plaintiffs and the defendant agree that there are two forms of ALS: familial, which compromises approximately 20% of ALS patients and is associated with genetics; and sporadic, which has no known case. Ratner Opinion 9. As Mr. Allen had no known family history of ALS, the plaintiffs' experts agree (and the defendants do not dispute) the decedent developed Sporadic ALS. Ratner Opinion 33, Oliver Opinion 10.

II. Synopsis of Expert Opinion

A. Opinion of Dr. Marcia Ratner

The crux of Dr. Ratner's opinion regarding general causation is: given evidence that ALS causes neuronal cell death and given evidence that toluene (or other chemicals) causes neuronal cell death, the two occurring simultaneously will result in more rapid neuronal cell death, thus hastening the effects of the disease. Deposition of Dr. Marcia Ratner 111 (Hereinafter "Ratner") (See attached "Exhibit E") ("it is just a matter of two plus two equals four"). According to Dr. Ratner: ALS is a neurodegenerative disorder associated with loss of motor neurons that is mediated by in part by oxidative stress and in part by glutamate mediated excitotoxicity which collectively lead to cell death via induction of apoptosis (programmed cell death). Ratner Opinion 32. It logically follows that exposure to chemicals that increase oxidative stress or glutamate-mediated excitotoxicity will hasten both the onset and the clinical course of ALS. Ratner Opinion 32.

Dr. Ratner's conclusion that this combined effect specifically caused the hastening of Mr. Allen's ALS is allegedly evidenced by three major factors. First, Mr. Allen and several co-workers reported exposures to chemicals at concentrations that were allegedly at least high enough to cause acute symptoms including dizziness, nausea and headaches. Ratner Opinion 32. Dr. Ratner therefore opined "with a reasonable degree of medical certainty" that the exposures were high enough to alter neuronal functioning as dizziness is allegedly a symptom of this. Id. Dr. Ratner secondly concluded that based on studies which determined the average age of sporadic ALS to be 60, and that given the fact that Mr. Allen experienced his first overt symptoms at approximately 45 years of age, the age of onset in the decedent's case was atypical. Ratner Opinion 33. Finally, Dr. Ratner concluded the alleged chemical exposure was a substantial contributing factor given the close temporal proximity to the diagnosis of ALS. Ratner Opinion 33. The factors in conjunction with one another led Dr. Ratner to conclude to a reasonable degree of medical certainty that Mr. Allen's ALS was hastened by exposures during the resurfacing of the field house floor. Ratner Opinion 33.

LEGAL ARGUMENT

I. Summary Judgment Standard

Federal law controls the procedural aspects of a diversity case, and therefore the grant of summary judgment is controlled by Fed.R.Civ.P. 56, as interpreted in the federal courts. Hammer v. Slater, 20 F.3d 1137, 1140 (11th Cir. 1994).

The "judge's function" at the summary judgment stage is to determine whether there is a "genuine issue for trial." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 249 (1986). "Where the record taken as a whole could not lead a rational trier of fact to find

for the non-moving party, there is no genuine issue for trial." Matsushita Electric Industrial Co. v. Zenith Radio Corp., 106 S.Ct.1348, 1356 (1986); accord Liberty Lobby, *supra* ("[T]here is no issue for trial unless there is sufficient evidence favoring the nonmoving party for a jury to return a verdict for that party."). It follows that "some metaphysical doubt as to the material facts" will not suffice to forestall summary judgment. Matsushita, *supra.* Similarly, "[t]he mere existence of a scintilla of evidence in support of the [non-moving party's] position will be insufficient." Liberty Lobby, 477 U.S. at 252.

II. Expert Testimony is Required to Prove Medical Causation

The question of whether expert testimony is required is a substantive one, and federal courts operating under diversity jurisdiction apply state law on the issue. In Re Paoli R.R. Yard PCB Litig., 35 F.3d 717, 751 (3d Cir. 1994). In cases of medical causation, proof of causation must rest upon expert medical testimony as it is beyond the knowledge of the ordinary layman. Theresa Canavan's Case, 432 Mass. 304, 316 (2000); Hachadourian's Case, 340 Mass. 81, 85 (1959).

For reasons set forth below, the plaintiff's experts must be excluded pursuant to Daubert. It is well established that where expert testimony is required, summary judgment must be granted on those claims for which the plaintiff is unable to provide such expert testimony. See Polaino v. Bayer Corporation, 122 F.Supp.2d 63 (D.Mass 2000). As the plaintiff has failed to produce expert testimony in regard to the issue of causation by the defendants, summary judgment must be granted.

III. Gate Keeper Function of the Court Regarding Scientific Opinion Evidence

When determining whether to admit expert testimony, duty of trial judges is to play the role of "gatekeeper," insuring that fact-finding process does not become distorted by what is popularly called "junk science," and this role is especially sensitive in cases where the plaintiff claims that exposure to toxic substance caused his injury as a jury may blindly accept expert's opinion that conforms with their underlying fears of toxic substances without carefully understanding or examining basis for that opinion. Whiting v. Boston Edison Company, 891 F.Supp.12, 24 (D.Mass 1995) (hereinafter "Whiting"); citing O'Connor v. Commonwealth Edison Co., 807 F.Supp. 1376, 1391 (C.D.Ill. 1992).

In Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993) (hereinafter "Daubert"), the Supreme Court established guidelines for district courts to use in determining the admissibility of expert testimony pursuant to Rules 702 and 104 of the Federal Rules of Evidence (FRE). Although it recognized that the evaluation of expert testimony is generally left to juries, the Court emphasized the trial judge's "gatekeeping" role with respect to expert proof on scientific issues. Id. at 597-98 (citing FRE 104(a)).

Currently two gateposts frame the exercise of a judge's discretion. First a witness must be shown to be sufficiently qualified by "knowledge, skill, experience, training, or education" before he will be permitted to give expert testimony. Whiting at 24 quoting Fed.R.Evid. 702. Second, the court must establish "any and all scientific evidence admitted is not only relevant, but reliable." Id. quoting Daubert at 589.

The advisory committee notes to FRE 702 explain other factors that a court may consider, including: (1) whether the experts are "proposing to testify about matters growing naturally and directly out of research they have conducted independent of litigation, or whether they have developed their opinions expressly for the purpose of testifying; (2) whether the expert has unjustifiably extrapolated from an accepted premise to an unfounded conclusion; (3) whether the expert has adequately accounted for obvious alternative explanations. Advisory Committee Notes to Fed.R.Evid.702.

IV. Dr. Ratner Does Not Have Sufficient Knowledge, Skill, Experience, Training or Education Related to the Subject Matter at Hand, and is Therefore Not Qualified to Make an Expert Opinions

Dr. Ratner does not have sufficient knowledge, skill, experience, training, or education related to the subject matter at hand, and therefore are not qualified to make an expert opinion.

Federal Rule 702 provides: If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise. Akerson v. Falcon Transport Co., Slip Copy 2006 WL 3377940, 4 (D.Me.);Taylor v. Airco, Inc., 494 F.Supp.2d 21, 22 (D.Ma 2007).

A witness must be qualified in the *specific* subject for which his testimony is offered. Whiting at 24. "Just as a lawyer is not by general education and experience qualified to give an expert opinion on every subject of the law, so too a scientist or medical doctor is not presumed to have expert knowledge about every conceivable scientific principle or disease." Id.

To qualify as an expert under Rule 702, a witness must first establish his expertise by reference to "knowledge, skill, experience, training, or education." FRE 702. Although this requirement has always been treated liberally, liberal interpretation of this requirement "does not mean that a witness is an expert simply because he claims to be." In re Paoli RR Yard PCB Litigation, 916 F.2d 829, 855 (3d Cir. 1994).

Dr. Ratner received her Doctorate of Philosophy from the Behavioral Neurosciences Program at the Boston University School of Medicine in 2004. Ratner Curriculum Vitae, attached as "Exhibit G". Dr. Ratner's doctoral thesis focused on Parkinson's disease, age of onset, and its relation to chemical exposure. Ratner 18. Dr. Ratner completed a Post-Doctoral Fellowship at the Laboratory of Molecular Neurobiology in the Department of Pharmacology and Experimental Therapeutics, in which the concentration was aging. Ratner Curriculum Vitae, Ratner 6.

Although Dr. Ratner has general experience in the area of neuroscience, her knowledge with regard to ALS does not rise to the level of an expert with regard to the specific subject matter of this case. Dr. Ratner has not performed any research or participated in studies regarding ALS. Ratner 188. Dr. Ratner's only experience with ALS has been what she has studied during her educational training. Ratner 188.

Dr. Ratner appears to be in the position anticipated by the advisory committee while drafting FRE 702, that is, she is an expert hired to testify in regard to a novel theory that she had culminated specifically for this litigation. Advisory Committee Notes to Fed.R.Evid. 702. Dr. Ratner's experience with neurodegenerative diseases has focused primarily on Parkinson's disease and aging, and cannot be proficient as anticipated by Daubert to form such a nuanced theory on a disease she has not studied extensively.

Ratner 18, 6. Dr. Ratner all but stated that she only formed this theory for litigation at deposition. When questioned regarding how she determined that toluene was the source of Mr. Allen's development ALS before the mean age of onset, Dr. Ratner stated, "My opinion would be the same even if that guy died at 60 instead of 75 and had history of this exposure… but you wouldn't have bothered to depose me in that case…Somebody else has moved down from where they are to here. But it may not result in a lawsuit, and I wouldn't be here, because--- I wouldn't be here." Ratner 172-3.

Moreover, Dr. Ratner has attempted to testify to a reasonable degree of medical certainty throughout her opinion. Ratner Opinion 33 ("It can therefore be concluded with a reasonable degree of medical certainty that Mr. Allen would have been unlikely to develop overt symptoms of ALS at age 45-years-old and would not have died on May 16, 2004 had he not been exposed to the chemicals used in the gym floor refurbishment process."). Although Dr. Ratner may have a body of medical knowledge which she acquired during the pursuit of her doctorate degree, Dr. Ratner is not licensed to practice medicine in any state. Ratner 13-16. Dr. Ratner is therefore not qualified through her education to testify with any degree of medical certainty and should be precluded from testifying in that capacity.

Based on the aforementioned, Dr. Ratner's testimony should be precluded on the grounds that she is not qualified by education, knowledge, experience, skill or training in the specific area of ALS and its interaction with chemical exposures. FRE 702. Furthermore, Dr. Ratner's testimony should be precluded on the grounds that it is the product of this litigation and did not grow naturally and directly out of research she has conducted independent of litigation. Advisory Committee Notes to Fed.R.Evid.702.

V. Dr. Ratner's Opinion is Merely a Speculative Hypothesis Which Cannot Assist the Trier of Fact and is Therefore Inadmissible

In addition to requiring that a proposed expert's testimony be "reliable," Rule 702 requires that the expert's testimony assist the trier of fact. This requirement has been interpreted to mean that scientific testimony must "fit" the facts of the case, that is, there must be a connection between the scientific research or test result being offered and the disputed factual issues in the case in which the expert will testify. Daubert at 592. In short, under Daubert and its progeny, a party proffering expert testimony must show by a "preponderance of proof" that the expert whose testimony is being offered is qualified and will testify to scientific knowledge that will assist the trier of fact in understanding and disposing of issues relevant to the case. Id. at 592.

Expert testimony has no capacity to be of assistance to a jury in resolving the ultimate issues if it is ground on speculation shaped by result-oriented biases or is merely a hypothesis. Whiting at 25. Expert testimony must be excluded when it rests on unverified assumption, speculation and guesswork. Polaino v. Bayer Corporation, 122 F.Supp.2d 63, 69 (D.Mass 2000), (expert failed to thoroughly investigate facts upon which hypothesis was based in case regarding alleged toxic exposure). The purpose of excluding speculative evidence is well explained by the court in Johnston:

> "A hypothesis is synonymous with a theory. Consequently, any hypothesis or theory is not fact until it has been scientifically proven. Anyone who has been trained in the scientific method realizes that a hypothesis is a scientist's educated speculation... It is important to underscore again that a court of law is not a scientific experiment. When a court of law determines responsibility for human suffering and awards damages, it must do so based upon reasonable evidence, not just speculation or hypothesis. Just because scientists use hypotheses to describe something they really don't know for sure does not justify a court of law in using speculative hypotheses to determine that one person has caused harm to another."

Whiting at 25 quoting Johnston v. United States, 597 F.Supp.374, 393-4 (D.Kan.1984).

Scientific expert testimony introduces special dangers to the fact-finding process because it "can be both powerful and quite misleading because of the difficulty in evaluating it." Daubert, 509 U.S. at 595 (internal quotation marks and citation omitted). Therefore, "federal judges must exclude proffered scientific evidence under Rule 702 unless they are convinced that it speaks clearly and directly to an issue in dispute in the case, and that it will not mislead the jury." Cloud v. Pfizer, Inc., 198 F. Supp. 2d 1118, 1130 (D. Ariz. 2001) (citing Daubert II, 43 F.3d at 1321).

The court does not have to admit opinion evidence that is "connected to existing data only by the *ipse dixit* of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion preferred." Polaino v. Bayer Corporation, 122 F.Supp.2d 63, 67 (D.Mass 2000) (hereinafter "Polaino"); quoting General Electric Co. v. Joiner, 522 U.S. 136, 146 (1997). "Rather, trial judges may evaluate the data offered to support an expert's bottom-line opinions to determine if that data provides adequate support to mark the expert's testimony as reliable." Id. quoting Ruiz-Troche v. Pepsi Cola of Puerto Rico Bottling Co., 161 F.3d 77, 81 (1st Cir. 1998).

Furthermore, the burden is placed upon the Plaintiff to prove the two separate components of causation in a toxic tort case: general and specific causation. Whiting v. Boston Edison Co., 891 F.Supp. 12, 24 (D.Mass. 1995).

A. General Causation

Dr. Ratner's opinion as to general causation is nothing more than a speculative hypothesis which cannot assist the trier of fact, and should therefore be precluded.

Dispositively, as the state of science now sits, it is impossible to prove Dr. Ratner's theory of general causation. When reviewing whether Dr. Ratner's expert opinion has unjustifiably extrapolated from an accepted premise to an unfounded conclusion pursuant to the advisory committee notes provided with FRE 702, the most salient fact is that Dr. Ratner herself acknowledges that the only accepted premise in regard to the hastening of ALS is that there is no known cause of ALS. Ratner Opinion 9. It therefore follows that it is impossible to determine that any chemical or given variable hastens the effect of ALS, as all variables studied to date have at best given the lesser status of "associated" with the disease. Ratner 89 ("I think that there are some research that has made some associations between trauma, but I don't know that we can say that it is the cause of ALS any more than we cay say that anything else is the cause of ALS. The same thing, the loss of neurons associated with the trauma can additively interact with the loss of neurons associated with the neurodegenerative disease process"), 154 ("again, there are studies that have associated ALS with quite a few things… with running, with infection, with trauma"). Critically, while there are peer-reviewed studies regarding the association between ALS and other variables (ie trauma), even those topics which have been more thoroughly tested will not classify a connection as greater than "associated". Ratner at 89, 105, 108, 154, 158. At this stage of the scientific exploration of sporadic ALS, the only accepted theory regarding its onset is that there is no known cause. Ratner Opinion 9.

As will later be discussed in detail, Dr. Ratner's opinion is improper as it is *ipse dixit*. Polaino at 67. Dr. Ratner concurred that no studies have specifically made a connection between toluene and the hastening of ALS. Ratner 56, 100, 189, 116. Dr.

Ratner testified that the while there has been research on the toxic effects of toluene and research with regard to the progression of ALS, there has not been research performed let alone proving a connection. Ratner 55-6.

Secondly, Dr. Ratner's theory of general causation has not been expressed in terms which can assist the trier of fact in this matter. It is inappropriate because it does not speak clearly and directly to an issue in dispute in the case, and would therefore mislead a jury. Cloud at 1130. Namely, Dr. Ratner has no provided criteria by which the trier of fact can determine whether any event is the proximate or actual cause of the early onset of ALS.

Dr. Ratner has testified that sufficient quantities of toluene for sufficient durations of time can cause the hastening of ALS. Ratner 136-7. Dr. Ratner would not posit what these specific quantities were, but and stated that even smelling nail polish would have an effect on the age of onset. Ratner 137-8 ("Because sufficient means just that. Sufficient"), 139. Dr. Ratner testified the minimal amount and duration of exposure to toluene that a person susceptible to ALS must be exposed to would be "that which contributed to an increase in the body burden of free radicals Ratner 140. According to Dr. Ratner this figure would have to be determined experimentally, which she was not aware of having been performed yet. Ratner 140-141. Dr. Ratner additionally testified that toluene is ubiquitous and is found even in everyday household cleaning supplies. Ratner 85. Based on Dr. Ratner's specificity, there would be no means by which to determine that an exposure was the actual and proximate cause of patients allegedly hastened ALS, as every ALS patient undoubtedly was exposed to toluene on numerous occasions throughout his lifetime and any given exposure may have been "sufficient".

To further confuse the matter, Dr. Ratner agrees that toluene is not the only outside contributing factor to the progression of ALS. Dr. Ratner testified that everything in an individual's life, experienced prior to and following an onset of symptoms, in some way contributes to the progression of the disease. Ratner 105. Dr. Ratner also testified that an increase in oxidative stress likely hastens the onset and progression of ALS, and that an increase in oxidative stress can occur as a result of such regular activities as eating food. Ratner 112. Other factors which, unlike toluene, have been peer reviewed that contribute to ALS by the same means which she concludes that toluene contributes to ALS include trauma, hypertension, medications including steroids, and viral infections. Ratner at 89, 105, 108, 158. Dr. Ratner distinguishes no means by which a trier of fact can distinguish what activities or exposures are the actual and proximate cause of the hastening of ALS.

Although she has given great weight to it in her opinion, Dr. Ratner has additionally not provided criteria to assist the trier of fact in determining whether the temporal proximity of an exposure to the presentment of symptoms has significance. Dr. Ratner testified the time of neuronal loss may not be significant when she stated "if he had a head injury at six years old it may still contribute to the age of onset of ALS, but that interaction wouldn't occur until you are 45 or 50 years old... if you had the trauma at 45 years old, that interaction may be almost instantaneous because the loss of neurons had reached a point where you would push it over the edge by losing just a few more where the symptoms would become overt." Ratner 165. Dr. Ratner testified that no peer reviewed studies exist that conclude that following an exposure to toluene, an individual with ALS would develop symptoms within a certain period of time. Ratner 162.

In sort, Dr. Ratner's theory should be precluded on the grounds that it is merely speculative and based on a tenuous connection between studies which have drawn conclusions regarding the pathology of ALS and studies which have drawn conclusions regarding the pathology of chemical exposures which to not meet the "fit" requirements of Daubert. See Daubert at 592, Polaino at 67. Dr. Ratner has failed to drawn opinions which speak clearly and directly to the issue of causation in this matter, and should be precluded from expressing these opinions on the grounds that she would confuse rather than assist a jury in this matter. See Daubert II at 1321, FRE 702.

B. Specific Causation

Dr. Ratner's opinion in regard to specific causation is merely a hypothesis which does not satisfy the "fit" requirements of Daubert and will not assist the trier of fact. Dr. Ratner's opinion should therefore be precluded. Polaino at 67, Daubert at 592.

As a preliminary matter, Dr. Ratner cannot conclude that the progression of Mr. Allen's ALS was hastened by his exposure to toluene, as both Dr. Ratner and the science community generally have made clear that there are no known causes of ALS, nor has Dr. Ratner pointed to any studies conclude factors which exacerbate ALS. Ratner Opinion 9. Dr. Ratner's opinion is improper because it connects the existing data only by *ipse dixit*, leaving too great an analytical gap between the data and the opinion proferred. Polaino v. Bayer Corporation, 122 F.Supp.2d 63, 67 (D.Mass 2000). Dr. Ratner simply cannot prove a connection between the hastening of ALS and exposure to toluene while ALS research remains in an infantile stage and while its pathology remains uncertain.

Dr. Ratner's opinion on specific causation was summarized when she stated, "The only thing we can say for sure is that he was asymptomatic before the exposure. He is

exposed, and he becomes symptomatic. I have a chemical he was exposed to in concentrations high enough to cause overt symptoms, and the chemical has mechanisms of toxicity that have been implicated in ALS." Ratner 163. Assuming, in arguendo, Dr. Ratner's speculative theory with regard to general causation is true, that is, that exposure to toluene at sufficient concentrations and durations could hasten the course of ALS, Dr. Ratner has failed to otherwise prove specific causation and therefore should be precluded from testifying. Whiting at 24 (must prove general and specific causation in toxic tort cases).

Dr. Ratner has proven specific causation first, because she not even estimated the amount or duration Mr. Allen's exposure. Dr. Ratner testified that Dr. Ratner has testified that sufficient quantities of toluene for sufficient durations of time can cause the hastening of ALS. Ratner 136-7. Dr. Ratner testified of her own volition that it was impossible to determine the quantities of toluene to which Mr. Allen was exposed. (Ratner Depo 59, 116, 200). Dr. Ratner agreed that these concentrations and durations which Mr. Allen suffered from were only determined to be sufficient based on Mr. Allen's assertion that he experienced such symptoms as dizziness, headache and nausea following his alleged exposure. Ratner 139. Nonetheless, Dr. Ratner rebutted her own theory when she agreed that her "reliance on the reports of Mr. Allen's symptoms [was] merely anecdotal rather than scientific, reliable evidence such an indoor air quality test." Ratner 196. By admitting her testimony is speculative, Dr. Ratner has therefore proven that she is not able to make a connection between the test result being offered (that Mr. Allen had a sufficient quantities and durations of toluene to hasten the course of ALS) and the disputed factual issues in the case (whether chemicals used during the

resurfacing of the fieldhouse floor were the cause of the "early onset" of Mr. Allen's ALS). Daubert at 592.

Secondly, Dr. Ratner has not proved that toluene, and not other potential factors known to act "by the same means as toluene", was the specific cause of his "early onset." Pursuant to the advisory committee's notes to FRE 702, Dr. Ratner's testimony is unreliable on the grounds that she has failed to account for other obvious explanations.

Dr. Ratner met with Mr. Allen when he sought consultation with the Environmental and Occupational Neurology Program at BU for a possible toxic exposure related to neurological symptoms on April 13, 2004, nearly 3 years following his alleged toxic exposure. Ratner Opinion 7. Dr. Ratner supported her determination that Mr. Allen's ALS was subclinical prior to June of 2001 by stating "from everything we can find in his history, I don't see anything that was suggesting that he was having problems that he was seeking attention for prior to that." Ratner 32. Although Dr. Ratner claimed to have taken an occupational history and questioned Mr. Allen regarding his hobbies in order to determine other potential contributing factors to his ALS, it is clear from further testimony that she did not take into account a full history. Ratner 85.

Dr. Ratner testified that there were many potential factors that could have contributed to the progression of Mr. Allen's ALS, including trauma, viral illness, steroid use and hypertension, but declined to consider them as the specific cause of Mr. Allen's allegedly hastened ALS. Ratner 89, 105, 108, 112, 114-5, 150. Dr. Ratner opined that "everything in his life that he [Mr. Allen] experienced prior to the onset of his symptoms and since the onset of his symptoms in some way contributed to the progression of this disease", but Dr. Ratner arbitrarily assigns the greatest value in the hastening of his ALS

to his exposures at the field house. Ratner 105, 169.Dr. Ratner attempted to explain her reasoning when she testified,

> As I said, I am not saying the chemicals caused ALS. I am not saying that viral factors caused ALS. I am not saying that running causes ALS. All these things collectively can contribute and modify the course of the disease in various ways. But among the factors in his life that were most likely to have a marked impact on his age of onset is this factor [toluene]. The position of the Occupational Safety and Health Administration[1], the exposure to levels that he was exposed to causing overt symptoms he complained of, all these factors taken together leave me unable to state with a reasonable degree of medical certainty that toluene did not play a role in this case. It absolutely did. And in my opinion, the only argument is..to what extent. Not if, but to what extent. And I think that it is a considerable extent. I just do not believe, given everything that stands in front of me, that this guy would have developed ALS two standard deviations below the mean but for this exposure. Ratner 169-170.

Dr. Ratner also tried to explain her emphasis on the alleged chemical exposure over other factors when she stated,

> And I have got this one salient thing in his life that stands out that was not typical, and that is his exposure to a known neurotoxicant that occurred in chronologic relationship to the onset of his disease, that shared mechanisms in common with that associated with ALS, and that the exposure was documented, the levels that occurred were high enough to cause acute symptoms. I have to ascribe a considerable amount of weight to the value of the exposure. And those other factors, I don't completely discount them, but I don't think they are as heavy of factors in this case." Ratner 153-4.

It is clearly from her testimony that there is an inexcusable analytical gap between the facts of this case and her opinion as to specific causation, and that her opinion is merely a speculative hypothesis shaped on a result-oriented basis. Whiting at 25, Polaino at 67 and 69. First, Dr. Ratner uses assertions which she herself has agreed have not been proven and are thus speculative. Dr. Ratner has testified, as explained above, that she

[1] It should also be noted that the courts have found that the fact that a substance has been classified as a carcinogen by agencies responsible for public health regulations is not probative of the question of whether a specific disease was caused by an exposure. Allen v. Pennsylvania Engineering Corp., 102 F.3d 194, 194 (5th Cir. 1996).

could not determine the amount or duration of Mr. Allen's exposure and that her evidence regarding his acute symptoms is merely anecdotal. Ratner 59, 116, 200, 196. Secondly, although Mr. Allen may have alleged feeling dizziness and nausea following his alleged exposure, he also reported trauma (torn rotator cuff), hypertension, and symptoms of viral illness prior to the onset of his ALS, all which Dr. Ratner has admitted *have* been scientifically studies as associated with the onset of ALS. Ratner 89, 105, 108, 112, 114-5, 150. Finally, Dr. Ratner expresses speculation in her own explanation when she above testifies she does not know to what extent the toluene hastened the onset of Mr. Allen's ALS, and it is in appropriate for her to speculatively testify that she "thinks" it was to a "considerable" extent, at term which she is unable to define. Ratner 169-174.

Thirdly, Dr. Ratner testified that her opinion as to specific causation may have been different had she performed tests which were should have been routine. Dr. Ratner testified that to the best of her knowledge, a neuropsychological examination was not performed because Mr. Allen did not complain of cognitive problems. Ratner 96. However, Dr. Ratner attested that there are studies that identify cognitive deficits caused by an exposure to toluene and that cognitive deficits are a common result of exposure. Ratner 97. Dr. Ratner agreed that the results of a neuropsychological examination would affect her opinion. Ratner 98. These facts both support that Dr. Ratner drew her conclusions based on speculative reasoning, and indicate that her opinion regarding Mr. Allen's toluene exposure was formed during pending litigation rather than at the time Mr. Allen was examined when she could have performed further tests which may have suggested a different conclusion.

For the above mentioned reasons, Dr. Ratner's conclusions as to specific causation in this matter cannot assist the trier of fact, as they are based upon speculative reasoning, result-oriented biases and unverified assumptions. Polaino at 69. Dr. Ratner's testimony should therefore be precluded..

VI. The Connection Between Toluene and the Hastening of ALS is Not Reliable Under the Four Factors Suggested by Daubert, and Should Therefore be Precluded.

The connection between toluene and the hastening of ALS is not reliable under the enumerated factors in Daubert, and expert testimony regarding their connection should therefore not be held admissible on these grounds.

In deciding whether an expert's testimony is reliable, the court may consider whether the theory 1) has been subjected to publication and peer review; 2) has been tested; 3) has a known rate of error; and 4) has general acceptance in the relevant discipline. Daubert at 593-4.

Establishing medical causation requires application of the scientific method that is, the generation of a testable hypothesis that is then subjected to the real-world crucible of experimentation, falsification/validation, and replication. See Daubert at 593. In this instance the applicable medical field of study is Epidemiology. Epidemiology is defined as the field of public health and medicine that studies the incidence, distribution, and etiology (cause) of diseases in society. The purpose of epidemiology is to better understand disease causation and to prevent disease in groups of individuals.

In toxic tort cases, the methods and techniques of epidemiology provide scientifically accepted means of assessing the relationship between exposure

to an agent and the potential health consequences. Allen v. Perm. Eng'g Corp. 102 F.3d 194, 197 (5th Cir. 1.996) ("the most useful and conclusive type of evidence in a case such as this is epidemiological studies"); Sutera v. The Perrier Group of Am., Inc., 986 F, Supp. 655, 662-63 (D. Mass. 1997) (lack of epidemiological evidence supporting causal relationship between exposure to substance and claimed disease key factor in exclusion of expert's causation opinion). It cannot be concluded that the expert's mere assertion that a methodology is reliable is sufficient to pass the Daubert test absent any other evidence showing its reliability. Id. referring to Kumho Tire Co. v. Carmichael, supra at 157.

A. A Connection Between Toluene Exposure and the Hastening of ALS Has Not Been Subjected to Peer Review and Publication

Although Daubert has enumerated peer review and publication as one factor useful in determining reliability of expert opinions, the plaintiff's own expert has made clear that her opinion has not been subject to these mediums. Daubert at 593. At deposition, Dr. Ratner unambiguously testified that her specific opinion had not been subject to peer review, nor had it been submitted to publication. Ratner at 21, 79, 83, and 101. No further elaboration is necessary regarding this expert's lack of peer review.

B. A Connection Between Toluene Exposure and the Hastening of ALS Has Not Been Tested and Therefore Does Not Have a Known Rate of Error

Daubert further suggests reviewing whether a theory has been tested and has a known rate of error as a means of determining reliability. Daubert at 594. Daubert and its progeny make clear that "[p]roposed [expert] testimony must be supported by appropriate validation." Daubert, 509 U.S. at 591. See Daubert, 509 U.S. at 593 (emphasizing the district court's role as a "gatekeeper" and stating that valid scientific methodology usually involves "generating hypotheses and testing them to see if they can

be falsified"); Smelser v. Norfolk Southern Ry. Co., 105 F.3d 299, 304 (6th Cir. 1997) (applying Daubert to exclude the testimony of a biomechanical engineer who failed to conduct pertinent testing). Dr. Ratner testified at deposition that her specific theory had not been tested. Ratner 55-6. Therefore it cannot have a known rate of error.

Dr. Ratner referred to "statistical power" as one means by which to test the reliability of a theory. Ratner 75. Dr. Ratner testified that in a single case study, the criteria does not apply. Id. Dr. Ratner opined that an N of 1 in this case was sufficient despite her conjecture that studies usually require an N of 8 if they expect 50% difference in responding with 25% variance. Ratner 76-78. For reasons discussed herein this memorandum; including the Dr. Ratner's inability to quantify the amounts of toluene to which Mr. Allen was exposed, her inability to determine the effect which any exposure may have had, her inability to eliminate other factors which have been associated with ALS, and her inability to make a sufficient bridge between known pathology of both ALS and known pathology of toluene; Dr. Ratner's optimism that a single case study is sufficient to prove general causation in this matter is unfounded. Courts have also found an "N of 1" to be insufficient in proving general causation. See Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d 1311, 1321 (9th Cir. 1995) (on remand) ("a relative risk of less than two…actually tends to disprove legal causation."), Pick v.Am. Med. Sys., Inc., 958 F. Supp. U 51, 1160 (E.D. La. 1997) (relative risk of 2.0 implies (on the average) there is a 50% likelihood that a particular case of the disease was caused by the event under investigation and a 50% likelihood that the disease was caused by chance alone; study finding lower relative risk may be insufficient to support verdict on causation); Landrigan, 605 A.2d at 1087 (relative risk greater than 2.0

required lo support causal inference between exposure and disease). Landrigan v. Celotex Corp., 605 A.2d 1079, 1087 (N.J. 1992) (relative risk greater than 2.0 "supports an inference that the exposure was the probable cause of the disease and a specific member of the exposed population.").

Dr. Ratner attested studies supporting her opinion allegedly independently show how toluene can cause neurological dysfunction, show how ALS causes cells to die and show how "toluene mechanisms of action can interact with the mechanisms of action of ALS to hasten the progression of the disease." Ratner 55. More importantly, Dr. Ratner testifies that no studies conclude that toluene hastens the progression of ALS. Ratner 56.

Dr. Ratner testified that "there are studies that have looked at, in animal models, the interactions between chemicals and ALS, and toluene is a chemical. And they have looked at the interaction as far as slowing the progression and hastening the progression of the disease. So in that regard, this topic is being studied extensively..." Ratner 100. Nonetheless, Dr. Ratner stated that there are no specific animal studies that focus on the effects of toluene hastening ALS. Ratner 100. Moreover, Dr. Ratner testified generally that "the relationship between toluene and ALS specifically has not been reported." Ratner 189.

Dr. Ratner agreed that "studies looking at an association between the prevalence of incidence of ALS have failed to find a significant association between exposure to any specific neurotoxic chemical and the occurrence of the disease. Ratner 116. Given Dr. Ratner's testimony, it is clear her opinions have not been tested by others and do not have a known rate of error, failing yet another Daubert factor.

C. A Connection Between Toluene Exposure and ALS is Not Generally Accepted Within the Scientific Community.

The fourth enumerated factor in Daubert suggested to determine the reliability of expert testimony was whether a theory was generally accepted within scientific community. Daubert at 594. Dr. Ratner herself resolved this issue when she testified that her theory was "novel". Ratner 81.

Dr. Ratner testified that she had submitted her opinion to the Harvard School of Public Health in hopes of discussing it at Grand Rounds. Ratner 79. She testified, "this [theory] is pushing the envelope of medicine, so Grand Rounds is a place where physicians come to think about novel ideas, what is pushing the envelope, where we are going with research. Ratner 81. Dr. Ratner, through her own verbiage, has eliminated the fourth enumerated factor used in Daubert to resolve expert reliability.

CONCLUSION

Based on the aforementioned and the arguments set forth in Defendants' Daubert Motion for Summary Judgment and/or to Preclude Plaintiff's Expert Testimony of Dr. Christine Oliver, the Defendant, Southwest Recreational Industries, Inc. hereby moves this Honorable Court to grant summary judgment in its favor and to preclude the Plaintiff from introducing the opinion of expert witness Dr. Marcia Ratner.

Dated: November ____, 2007

Respectfully submitted,
The Defendant,
Southwest Recreational
Industries, Inc.,
By its attorney,

_____
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EXHIBIT A

UNITED STATES DISTRICT COURT
FOR THE
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY; And As ADMINISTRATRIX OF THE ESTATE OF DANIEL ALLEN; And AS NEXT FRIEND OF TAYLOR ALLEN AND DANIELLE ALLEN; And MARK ALLEN,	
Plaintiffs;	**CIVIL ACTION No.: 05-40048**
v.	
MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES; And SOUTHWEST RECREATIONAL INDUSTRIES, INC., d/b/a MARTIN SURFACING;	
Defendants.	

THIRD AMENDED COMPLAINT AND DEMAND FOR TRIAL BY JURY

INTRODUCTION

1. Plaintiffs bring this civil action against Defendants Martin Surfacing. a division of Southwest Recreational Industries, Inc.; Southwest Recreational Industries. Inc. d/b/a Martin Surfacing, 701 Leander Drive, Leander, TX 78641 (hereafter referred to jointly and severally as "Defendants") demanding damages, including punitive damages for the wrongful death of the late Daniel Allen.

2. Each Plaintiff individually and/or in their representative role demands damages in an amount deemed just and reasonable. Demand is also made for all compensation available

under the so-called Wrongful Death Statute G.L. c. 229, §2 et seq. Plaintiffs incorporate by reference and rely upon G.L. c. 229, §2 et seq.

3. The Defendants negligence, gross negligence and/or breach of express and/or implied warranty (including but not limited to Article 2 of chapter 106) and/or violations of M.G.L. 93A (hereafter collectively referred to as "wrongful conduct") directly and proximately caused the Late Daniel Allen to suffer related injuries, exacerbation of pre-existing injuries that were quiescent prior to Defendants conduct (hereafter "injury" or "injuries") and/or other loss including wrongful death. In turn, each Plaintiff suffered related damages arising out of the illness and wrongful death of the Late Daniel Allen.

4. The Defendants' wrongful conduct caused the late Daniel Allen to be exposed to toxic fumes, toxins, chemicals, volatile organic compounds and other hazardous and noxious airborne irritants and substances resulting from Defendants' processes and/or resurfacing of the "field house" floor at the College of the Holy Cross, Worcester Massachusetts (hereafter Holy Cross) during and/or subsequent to May of 2001.

5. The late Daniel Allen was the former Holy Cross Head Football coach.

6. Other losses suffered by Plaintiffs include the value of the loss of reasonably expected net income of the decedent, services, protection, care, assistance, society, companionship, comfort, guidance, counsel and advice. The Late Daniel Allen suffered extreme conscious pain and suffering, loss of net income, a diminution in earning capacity, exacerbation of a pre-existing condition, toxic poisoning, chronic fatigue, chemical neuritis, neurological abnormalities, and associated psychological and emotional distress including his eventual wrongful death. Related funeral and burial costs were incurred.

7. The Decedent's spouse and children each suffered severe psychological trauma resulting from directly witnessing or experiencing the effects of Defendants' wrongful conduct and this witnessing or experiencing followed closely the happening of the negligent act, both in time and place. The Defendants engaged in grossly negligent conduct which resulted in the death of Daniel Allen, and punitive damages must be assessed in an amount not less than $5,000.

8. Plaintiff Laura Allen is a natural person and a resident of the Commonwealth of Massachusetts, Worcester County. She is a natural person residing at 2 Sawmill Drive, Westborough, Massachusetts 01581.

9. At all times relevant to this complaint, Laura Allen was the lawful wife of the late Daniel Allen and the mother of his only three children. The late Daniel Allen's children Mark Stewart Allen (DOB May 29, 1985), Taylor Benjamin Allen (DOB January 13, 1990) and Danielle Lee Allen (DOB July 19, 1992) were all minors during the period of his conscious pain and suffering and wrongful death.

10. Plaintiff Mark Allen is an adult child of Daniel and Laura Allen, and maintains this Action on his own behalf as a co-plaintiff.

11. On or about December 6, 2004, Plaintiff Laura Allen was appointed Executrix of the Estate of the late Daniel Allen by the Probate Court of the County of Worcester, Commonwealth of Massachusetts, Docket No. 04 P3148EP1. Plaintiff Laura Allen is duly authorized to maintain this action in that capacity.

12. Laura Allen brings this action individually for her own loss and as the Executrix of the Estate the late Daniel Allen.

13. Laura Allen also acts as the next best friend of Taylor Allen and Danielle Allen. Each of these minor children of Laura Allen and the decedent reside with their mother in Westborough, Worcester County, Massachusetts. All Plaintiffs demand, in addition to their share of the damages awarded to the statutory beneficiaries, to be given fair and reasonable compensation for their own individual claims for emotional distress.

14. Defendant Southwest Recreational Industries, Inc. d/b/a Martin Surfacing, is a corporation with a principal place of business at 701 Leander Drive, Leander, TX 78641. As set forth in the next paragraph, Southwest Recreational Industries, Inc. is bankrupt.

15. The Defendants contracted with the College of the Holy Cross for certain goods and services, by which the Defendants were to have installed a new flooring system in the Holy Cross Field House (the "field house") during 2001.

16. The Defendants knew, or in the exercise of reasonable care should have known, that the chemicals and solvents used in the vicinity of Daniel Allen were toxic to humans who were in proximity to the fumes and byproducts of those chemicals and solvents.

17. At no time leading up to their commencement of the work referenced did the Defendants inform or warn any employees or agents of Holy Cross or the late Daniel Allen that the substances used and/or processes employed by them to resurface the field house floor pose a danger to the health of human beings occupying the building, or that they should take safety precautions, or leave the building during the resurfacing process because the substances and/or processes they would be using to resurface the field house floor pose a danger to the health of human beings occupying the building.

18. Notwithstanding their knowledge of the dangers and their notice of the defect, during the course of refinishing the field house floor, the Defendants failed to take adequate

measures to provide an adequate clean air supply, circulation or ventilation for the late Daniel Allen.

19. While carrying out the refinishing work, the Defendants failed to warn or inform the late Daniel Allen in any manner of the volatile organic chemicals and/or the other toxic, hazardous, harmful or noxious airborne irritants and substances and/or processes they caused to be present.

20. The defective product sold, installed, applied and used by the Defendants was used and installed in such a way as to make it avoidably unsafe, inasmuch as a simple warning and exclusion of unprotected people from the vicinity of the application would have avoided the consequences suffered by Daniel Allen.

21. The conduct of the Defendants constituted gross negligence.

22. The late Daniel Allen never knew anything about the fact that he was exposed to ultra-toxic chemicals until after he was exposed and became ill.

23. While refinishing the field house floor the Defendants' employees utilized protective gear including facial masks.

24. Certain constituents of the materials utilized by the Defendants to resurface the floor as above alleged contain chemicals and solvents such as Benzene and/or Isocyanates, which are classified as ultra-hazardous substances and/or processes in Massachusetts.

25. When the late Daniel Allen questioned the air quality issues associated with the Defendants refinishing work, the Defendants' agents, servants and/or employees assured him in a grossly negligent manner that he was in no danger and was exposed to no risk.

26. Subsequent air testing samples showed that the air at College of the Holy Cross field house contained chemical abnormalities related to the Defendants' hazardous products

and refinishing application process. This air testing confirmed the presence of Isophrone Diisocyanate as well as Benzene and other chemicals in the air.

27. By reason of Daniel Allen's wrongful death, the Plaintiff reasonably and necessarily expended the sum of $30,000 for funeral expenses.

COUNT ONE
General Negligence Claim

28. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs inclusive of this Complaint, with the same force and effect as if expressly set forth herein.

29. Despite their intimate knowledge regarding the dangers associated with exposure to Benzene and/or Isocyanates and/or the other volatile organic compounds and/or chemicals constituting or otherwise used in the application of their products, the Defendants used these ultra-hazardous materials in the contained field house building and failed to warn Coach Allen directly or indirectly of the danger presented to building occupants during use of these hazardous products.

30. Thus, in carrying out the refinishing of the field house floor, the Defendants engaged in negligent, grossly negligent conduct that resulted in the Plaintiffs' respective losses.

31. The Defendants knew or in the exercise of reasonable and ordinary care should have known that certain products and application processes they used in the installation of the field house floor contained Benzene and/or Isocyanates, volatile organic compounds, and other toxic and neurotoxic materials.

32. The Defendants should have taken reasonable steps to exclude persons who were unprotected from exposure to the toxic and neurotoxic materials they were using from the area of potential harm.

33. The defendants failed to take reasonable steps, and breached their duty to Daniel Allen.

34. As a direct result of the Defendants' failures to act and/or wrongful conduct, the late Daniel Allen suffered severe, permanent lethal personal injures and consciously endured great pain and suffering.

WHEREFORE, as a result of the Defendants' negligent, grossly negligent conduct, the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand damages in an amount deemed just and reasonable together with interests and costs against each of the Defendants jointly or severally.

COUNT TWO
Negligent Failure to Warn

35. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs inclusive of this Complaint, with the same force and effect as if expressly set forth herein.

36. The Defendants then failed to properly warn, eliminate, minimize, or supervise the application in such a way to provide for the safety and well being of Coach Allen. In doing so, the Defendants' wrongfully engaged in negligent and grossly negligent conduct.

37. The danger presented by the toxic flooring and application/curing in issue was not obvious to the late Daniel Allen and the late Daniel Allen was not already aware of said danger.

38. The Defendants provided no warning as to the toxicity in issue. The adequacy of the warning was otherwise defective because it was unduly delayed, reluctant in tone and lacking a sense of urgency.

39. The warning was otherwise defective because it was not comprehensible or conveyed to the average person and failed to convey a fair indication of the nature and extent of the danger to a reasonably prudent person.

40. The warning was not provided to all persons who it is foreseeable will come into contact with and consequently be endangered by the product in issue. The Defendants had a duty to warn because they knew or should have known that the product in issue was dangerous and/or ultra hazardous.

41. The risks in issue were known and/or reasonably foreseeable at the time of the sale and/or could have been discovered by way of reasonable testing prior to marketing the product.

42. The Defendants at all times relevant hereto were engaged in the marketing, promotion, formulation, manufacture, marketing, distribution and sale of toxic gym flooring.

43. Defendants engaged in wrongful conduct and are liable in tort to the Plaintiffs for reasons including, but not limited to, the following:

a. The materials used to formulate the toxic gym flooring are unnecessarily dangerous and defective, unsafe and unreasonably dangerous for their intended and/or foreseeable uses.

b. In designing the manufacturing and/or application and/or curing process, and/or in manufacturing, testing, inspecting, applying, distributing and/or as otherwise alleged in this complaint they put into the stream of commerce a product in such an

unreasonably dangerous condition and/or a process so filled with risk and danger that it was likely to cause harm to persons thereof when being used for its intended use.

c. In distributing, promoting and selling the unnecessarily dangerous product not accompanied by adequate warnings of the toxicity that was known or reasonably should have been known and by violating their duty and obligation to provide adequate warnings of the dangers known or which should have reasonably been known to persons coming in proximity.

d. The product and process were and continue to be unaccompanied by proper warnings regarding all known or reasonably knowable potential side affects associated with the use of the unnecessarily dangerous product and the comparative nature, extent, severity, incidence and duration of such adverse affects.

e. The warnings given do not accurately reflect the signs, symptoms, incidence, scope or severity of the side affects, or identify appropriate testing, monitoring or remedial action.

f. The Defendants continue to negligently fail to communicate to persons coming in proximity or contracting with them information necessary for their purposes. This conduct placed and continues to place the consuming public at risk.

g. The Defendants failed to perform and continue to refuse to perform adequate testing that would have shown that the unnecessarily dangerous product to be safe in a public location.

h. As a result of this failure, full and proper warnings were not made and continue to not be made that would accurately and fully reflect the symptoms. scope and severity of health problems the unnecessarily dangerous toxic gym flooring can cause.

i. Each of the Defendants knew that the unnecessarily dangerous product, which was manufactured and supplied by the Defendants, would be used without further inspection and study for such defects and that given the resources of the consuming public and the College of the Holy Cross any reasonably anticipated inspection would have failed to detect the defects and they were reasonable in relying on the Defendants for same.

j. The Defendants and each of them expected and knew that their toxic gym flooring would be used as is. The toxic flooring was in fact received and applied without change in the condition in which it was first manufactured and sold.

k. The late Daniel Allen was a foreseeable person and user of the flooring product and used the product in its intended manner and suffered serious harm because of said use.

l. The unnecessarily dangerous toxic flooring manufactured and/or supplied by the Defendants are defective due to inadequate post-marketing warnings or instructions because, after the manufacturer knew or should have known of the toxicity and related risks of injury, they failed to provide adequate warnings to persons or consumers of the product and continued to aggressively promote the unnecessarily dangerous toxic flooring.

44. As a direct and proximate cause of the defective warning accompanying the unnecessarily dangerous toxic flooring as manufactured and/or supplied by Defendants and as a direct and proximate cause of their wrongful conduct, carelessness, outrageous conduct and/or other wrong doings and actions as described herein, Plaintiffs suffered and will continue to suffer injury, harm and economic loss.

45. The Defendants knew or reasonably should have known of the toxic flooring's defective nature, but continually failed to correct known defects.

46. The Defendants as manufacturers and distributors had a duty to warn of risks, hazards and/or adverse reactions of which they knew or had reason to know are inherent in the use of its products.

47. As a direct and proximate result of the defects in the warning accompanying the product sold and distributed by the Defendants, the late Daniel Allen was caused to seek medical attention, to undergo numerous diagnostic procedures for which Plaintiffs have incurred expenses and will incur expenses and damages, which expenses are capable of precise calculation.

WHEREFORE, as a result of the Defendants' negligent failure to warn of all known or appreciable risks, the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand damages in an amount deemed just and reasonable, together with interests and costs against each of the Defendants jointly or severally

COUNT THREE
LOSS OF CONSORTIUM AND FOR OTHER RELIEF AVAILABLE UNDER G.L. c. 229

48. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs inclusive of this Complaint, with the same force and effect as if expressly set forth herein.

49. Plaintiff Laura Allen resided with Daniel Allen prior to his death and was dependent upon said decedent for his reasonably expected net income, support and maintenance. She has otherwise suffered a related loss of consortium.

50. Mark Stewart Allen, Taylor Benjamin Allen, and Danielle Lee Allen were also dependent upon their father's income, services, protection, care, assistance, society, companionship, comfort, guidance, counsel and advice, at the time of the exposure related injury that resulted in his death, Dan Allen was 45 years of age, was in good health and was employed profitably as a college football coach.

51. Laura Allen herein acts as the next friend of Taylor Benjamin Allen and/or Danielle Lee Allen.

52. Mark Stewart Allen now acts on his own behalf inasmuch as he is no longer a minor, although at all relevant times he was a minor.

53. By reason of the Defendants' wrongful conduct, the decedent's wife and minor children, have been deprived of the decedent's net income, services, protection, care, assistance, society, companionship, comfort, guidance, counsel and advice, in their respective share in such estate, as the decedent might have reasonably accumulated during a natural life expectancy.

54. As a result of the individual wrongful conduct of each Defendant, the wife and children of the late Daniel Allen have suffered a loss of financial support and consortium and decedent's net income, services, protection, care, assistance, society, companionship, comfort, guidance, counsel and advice and will continue to suffer a related loss for the rest of their life due to the injuries and wrongful death of the rate Daniel Allen.

WHEREFORE, as a result of the Defendants' negligent and grossly negligent conduct, the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand damages to make them whole. Plaintiffs demand judgment in an amount deemed just

and reasonable, including punitive damages, for the wrongful death of the late Coach Daniel Allen, together with interests and costs against each of the Defendants jointly or severally.

COUNT FOUR
Conscious Pain and Suffering

55. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs inclusive of this Complaint, with the same force and effect as if expressly set forth herein.

56. As a result of the Defendants' wrongful conduct, the decedent suffered related injury and eventually a wrongful death. Prior to his death, the decedent endured great conscious pain and suffering for the three years leading up to his wrongful death.

WHEREFORE, as a result of the Defendants' negligent conduct, the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand damages to make them whole. Plaintiffs demand judgment in an amount deemed just and reasonable including punitive damages for the conscious pain and suffering of the late Daniel Allen, together with interests and costs against each of the Defendants jointly or severally.

COUNT FIVE
Wrongful Death Caused by Grossly Negligent Conduct

57. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs inclusive of this Complaint, with the same force and effect as if expressly set forth herein.

58. The Plaintiff Laura Allen is entitled to and brings this action based upon the death of Daniel Allen, pursuant to the so-called "Wrongful Death Statute," M.G.L. Ch. 229, § 2 and demands all related damages contained therein as allowed by law.

59. The actions of the Defendants that directly and proximately caused or resulted in the death of Daniel Allen were grossly negligent acts and as a result of said acts, caused Daniel Allen to be injured and was so wrongfully killed.

WHEREFORE, as a result of the Defendants' grossly negligent conduct, the late Daniel Allen was caused to die and the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand punitive damages. Plaintiffs demand judgment in an amount deemed just and reasonable including punitive damages for the wrongful death of the late Coach Daniel Allen, together with interests and costs against each of the Defendants jointly or severally.

COUNT SIX
Violation of M.G.L. c. 93A

60. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs inclusive of this Complaint, with the same force and effect as if expressly set forth herein.

61. Defendants were engaged in trade or commerce as defined by Massachusetts General Laws, Chapter 93A.

62. The Defendants do not maintain a place of business or keep assets within the Commonwealth of Massachusetts.

63. The Defendants knowingly and willfully sold a defective product and also defectively installed that product, and in doing so violated M.G.L. c. 93A, § 2.

64. Plaintiffs have been injured by reason of Defendants unfair or deceptive acts or practices.

WHEREFORE, as a result of the Defendants' willful or knowing unfair and deceptive acts or practices, the Plaintiffs each suffered loss as described and/or will continue to suffer Joss for their

rest of their lives and demand damages to make them whole. Plaintiffs demand judgment in an amount deemed just and reasonable, trebled plus reasonable attorney fees together with interests and costs against each of the Defendants jointly or severally.

COUNT SEVEN
Wrongful Conduct

65. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs inclusive of this Complaint, with the same force and effect as if expressly set forth herein.

66. The Defendants had a duty to perfom1 their refinishing work on the Holy Cross Field house floor with due care, in a good and workmanlike manner and in a manner which would not harm the late Daniel Allen and/or to ensure that those using its ultra-hazardous products would not cause him harm.

67. In carrying out their wrongful conduct, the Defendants breached their duty of due care to Plaintiffs by negligently training to perform, performing and/or supervising the refinishing work on the field house floor such that the late Dan Allen was exposed to hazardous chemical fumes, volatile organic compounds and other airborne substances from the work and was thereby caused to suffer injury and eventually wrongfully caused to die.

68. In carrying out their wrongful conduct, the Defendants also failed to otherwise eliminate, minimize or warn of the risks posed by its toxic product and application process.

69. The Defendants breached their duty of due care to Plaintiffs by negligently allowing their employees, agents or servants to use products containing, among other harmful volatile organic compounds or chemicals, Benzene and/or Isocyanates, in such close proximity to

the late Daniel Allen and in such concentrated amounts without adequate measures to provide adequate air supply, air circulation, and air ventilation.

70. The Defendants' wrongful conduct resulted in a breach of their duty of due care to Plaintiffs. Further wrongful conduct includes a failure to provide adequate protective barriers between their work and the late Daniel Allen.

71. The Defendants further breached their duty of care to Plaintiffs because as a result of their wrongful conduct they failed to warn or instruct the late Daniel Allen or any other Holy Cross official of the hazards presented to them by exposures to Defendants' ultra-hazardous materials, volatile organic compounds and other airborne irritants during the resurfacing.

72. The Defendants breached their duty of care by conducting their resurfacing in a poor, un-workmanlike and substandard manner.

73. The Defendants further breached their duty of care because their wrongful conduct resulted in their failure to conduct their resurfacing work in compliance with applicable state and Occupational Safety Health Administration (OSHA) standards, industry, corporate and/or safe building laws, regulation and codes.

74. As a direct and proximate result of the Defendants' wrongful conduct, the late Daniel Allen was exposed to fumes, toxins, chemicals, volatile organic compounds and other hazardous airborne irritants and substances and/or processes and was injured and caused to die thereby.

75. As a direct and proximate result of the Defendants' wrongful conduct, the late Daniel Allen was caused to suffer severe personal injury, was caused to be disabled, was caused great pain of body and mind, was caused great emotional, psychological harm, was

caused to incur great medical and hospital expenses and suffered a loss of earning capacity.

WHEREFORE, as a result of the Defendants' negligent and grossly negligent conduct, the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand damages to make them whole. Plaintiffs demand judgment in an amount deemed just and reasonable, including punitive damages for the wrongful death of the late Daniel Allen, together with interest and costs against each Defendant jointly or severally.

COUNT EIGHT
Strict Liability

76. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs inclusive of this Complaint, with the same force and effect as if expressly set forth herein.

77. In the ordinary course of their business, the defendants utilized toxic, dangerous and ultra-hazardous chemicals, solvents, materials and/or processes, and brought those chemicals, solvents, materials and/or processes into the area near the office of the late Daniel Allen.

78. The ultra-hazardous chemicals, solvents, materials and/or processes were under the control of the Defendants at all relevant times.

79. The business activities of the defendants related to the ultra-hazardous chemicals, solvents, materials and/or processes:

a. Consisted of a high degree of risk;

b. Established a likelihood that great harm would result from said business and activity;

c. Were not a matter of common usage;

d. Were ultra-hazardous activities or substances;

e. Were inappropriate to use or perform in close proximity to the late Daniel Allen.

80. As such the Defendants are strictly liable in tort for all damages and injuries to the Plaintiffs that were a direct or proximate result of such business and activities.

81. As a direct and proximate result of said business and activities of the Defendants, the late Daniel Allen was caused to suffer severe personal injuries, was caused to be disabled, was caused and will be caused great pain of body and mind, was caused great emotional and psychological harm, was caused to incur great medical and hospital expenses and suffered a loss of earning capacity and eventually wrongfully die.

82. The late Daniel Allen's family members likewise suffered related loss.

WHEREFORE, as a result of the Defendants' negligent and grossly negligent conduct, the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand damages to make them whole. Plaintiffs demand judgment in an amount deemed just and reasonable including punitive damages for the wrongful death of the late Coach Daniel Allen, together with interests and costs against each of the Defendants jointly or severally.

COUNT NINE
Breach of Express Warranty

83. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs of this Complaint with the same force and effect as if expressly set forth herein.

84. The Defendants and/or their agents or subcontracts expressly warranted to Holy Cross, the general public and the late Daniel Allen that the materials (and/or process) involved in the resurfacing of the Holy Cross field house were safe and fit for the use intended.

85. The Defendants and/or their agents or subcontracts impliedly warranted to Holy Cross, the general public-and the late Daniel Allen that the materials (and/or process) involved in the resurfacing of the Holy Cross field house were safe and fit for the use intended.

86. The late Daniel Allen was a person whom the Defendants might have expected to use the refinished areas at College of the Holy Cross including all areas of the field house.

87. The Defendants breached their warranties because the resurfacing process and materials they used at College of the Holy Cross field house floor were ultra hazardous and/or unsafe and/or not of merchantable quality and/or unfit for their intended uses and purposes.

88. The Plaintiffs and more specially, the late Daniel Allen were harmed and suffered loss after they reasonably relied on the warranties made by the Defendants.

89. As a direct and proximate result of their reasonable reliance on Defendants warranties and as a direct and proximate breach of warranties by the Defendants, the late Daniel Allen was caused to suffer severe personal injury, related loss, and eventually suffer a wrongful death. He was also caused to be disabled, was caused great pain of body and mind, was caused great emotional and psychological harm, was caused to incur great medical and hospital expenses and suffered a loss of earning capacity and incur funeral expenses.

WHEREFORE. as a result of the Defendants' negligent and grossly negligent conduct, the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand damages to make them whole. Plaintiffs demand judgment in an amount deemed just and reasonable including punitive damages for the wrongful death of the late Coach Daniel Allen, together with interests and costs against each of the Defendants jointly or severally.

COUNT TEN
Breach of Implied Warranty

90. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs of this Complaint, with the same force and effect as if expressly set forth herein.

91. The Defendants impliedly warranted prior to, during and following the referenced resurfacing that College of the Holy Cross was fit for habitation, occupancy and use and would be reasonably safe during the application and curing period of its toxic flooring product.

92. The Defendants expressly warranted prior to, during and following the referenced resurfacing that College of the Holy Cross was fit for habitation, occupancy and use and would be reasonably safe during the application and curing period of its toxic flooring product.

93. The Defendants knowingly and or willfully misrepresented the truth in this regard and otherwise breached said warranties as the College of Holy Cross field house area was not fit for habitation, occupancy and use and was unreasonably dangerous during and following the refinishing process.

94. The late Daniel Allen relied upon said warranties and had occupied and inhabited the College of the Holy Cross field house to his detriment.

95. As a direct and proximate result of the breach of warranty by the Defendants, the late Daniel Allen was caused to suffer sever personal injury, was caused to be disabled, was caused great pain of body and mind, was caused great emotional and psychological harm, was caused to incur great medical and hospital expenses and suffered a loss of earning capacity.

WHEREFORE, as a result of the Defendants' negligent, reckless conduct, the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand damages to make them whole. Plaintiffs demand judgment in an amount deemed just and reasonable including punitive damages for the wrongful death of the late Coach Daniel Allen, together with interests and costs against each of the Defendants jointly or severally.

COUNT ELEVEN
Negligent Infliction of Emotional Distress

96. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs of this Complaint, with the same force and effect as if expressly set forth herein.

97. The late Daniel Allen's spouse and children each suffered severe psychological shock resulting from directly witnessing or experiencing the effects of Defendants' wrongful conduct.

98. This witnessing or experiencing followed closely the happening of the negligent act, both in time and place.

99. The Defendants' negligent conduct caused the Laura Allen and the Allen children and the late Daniel Allen to suffer severe emotional distress.

WHEREFORE, as a result of the Defendants' negligent and or intentional conduct, the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand damages to make them whole. Plaintiffs demand judgment in an amount deemed just and reasonable including punitive damages for the wrongful death of the late Coach Daniel Allen, together with interests and costs against each of the Defendants jointly or severally.

COUNT TWELVE
Intentional Infliction of Emotional Distress

100. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs of this Complaint, with the same force and effect as if expressly set forth herein.

101. The Defendants engaged in extreme and outrageous conduct toward the Plaintiffs and the conduct was beyond the scope of acceptable conduct.

102. The Defendants intended and/or knew or should have known that their extreme and outrageous conduct would likely result in the Plaintiffs' suffering of emotional distress.

103. The Defendants' extreme and outrageous conduct caused Plaintiffs to suffer from emotional distress of a nature that no reasonable person could be expected to endure.

WHEREFORE, as a result of the Defendants' negligent and or intentional conduct, the Plaintiffs each suffered loss as described and/or will continue to suffer loss for their rest of their lives and demand damages to make them whole. Plaintiffs demand judgment in an amount deemed just and reasonable including punitive damages for the wrongful death of the late Daniel Allen, together with interests and costs against each of the Defendants jointly or severally.

COUNT THIRTEEN
Defective Design, Manufacturing and Distribution

104. The Plaintiffs repeat and reallege each and every allegation contained in the foregoing and subsequent paragraphs of this Complaint, with the same force and effect as if expressly set forth herein.

105. When the product left the manufacturer, it was defective in that the gravity of danger posed by the product was unacceptable according to the manufacturers own specifications and minimum accepted industry standards, the likelihood of the defect was

such that danger would arise, the feasibility of a safer alternative was readily available, the financial cost of an improved design was reasonable and is accepted by the Defendants, and that the adverse consequences of the product would result in harm to the Plaintiffs and that the adverse consequences could be eliminated by the Defendant.

106. The manufacturing process used by the Defendant was defective as were the inspection and testing.

107. The propensity of the problem as sold when compared with those the Defendants intended it to have admittedly results in the acceptance by the Defendant that the deviation from the design rendered the product defective.

108. The toxic flooring manufactured and/or supplied by the Defendants was placed into the stream of commerce in a defective and unreasonably dangerous condition and was unnecessarily dangerous.

109. The toxic flooring manufactured and/or supplied by the Defendants was placed into the stream of commerce in an unnecessarily dangerous condition and was unreasonably dangerous and more dangerous than an ordinary consumer would expect.

110. The toxic flooring manufactured and/or supplied by the Defendants was placed into the stream of commerce in an unnecessarily dangerous condition and more dangerous than the Defendants admit is a minimally acceptable condition.

111. As set forth in this Complaint and otherwise, the Defendants knew or should have known of the defective and unnecessarily dangerous condition but continued to manufacture, market, promote, sell and represent to the consuming public, and general public that the unnecessarily dangerous toxic flooring was safe.

112. They did this for the sole purpose of maximizing sales and profits at the expense of the public health and safety in conscience disregard of the foreseeable harm caused by the unnecessarily dangerous toxic flooring.

113. As a result of Defendants' practices, Plaintiffs have suffered actual damages in that they have purchased and had implanted the unnecessarily dangerous toxic flooring, which are dangerous and defective and not fit for their intended purpose.

WHEREFORE as a result of the Defendants' negligent, reckless conduct, the Plaintiffs suffered loss and will continue to suffer loss for the rest of their lives and demand damages to make them whole for past and future loss to the maximum extent allowed under the law. Plaintiffs demand judgment in an amount deemed just and reasonable, together with interests and costs against each of the Defendants.

PRAYERS FOR RELIEF

114. As a direct result of the Defendants' failures to act and wrongful conduct, the late Daniel Allen was caused to suffer severe and permanent personal injuries and eventually suffer a wrongful death. Each member of his family suffered other related loss including but not limited to a loss of consortium. Each Plaintiff individually and/or in their representative capacity demands judgment in an amount deemed just and reasonable as outlined above for their past and future loss. Each likewise makes demand to be made whole to the maximum extent allowed under the law together with interests, costs and punitive damages, if appropriate against each of the Defendants individually.

a. As to each Plaintiffs' loss of consortium, they pray that damages for the spouse's loss of consortium and for each child's loss of companionship be awarded as separate parts of a single damage award;

b. As to the-loss of financial support to the presumed beneficiaries, each Plaintiff requests that they be awarded compensation for their loss as separate parts of a single damage award recovered for the benefit of all statutory beneficiaries;

c. Because Laura Allen and each child suffered emotional distress in the form of severe psychological shock resulting from directly witnessing and experiencing the effects of the Defendants' wrongful conduct over the time period from exposure through the rapid deterioration and eventual death, said suffering not simply grief and anguish attendant upon the death of a family member but much more of the late Daniel Allen, each claims they be awarded their own individual damages;

d. Laura Allen and each child requests that they be awarded the fair monetary value and/or the value of the reasonably expected net income of the decedent in accordance with the statutory scheme enunciated in G.L. c. 229, §2;

e. Laura Allen and each child demands that they be awarded in a single sum damages for the conscious pain and suffering on the part of the decedent in accordance with G.L. c. 229, §6;

f. Laura Allen and each child demands that they be provided with compensatory damages for the fair monetary value of the decedent's net income, services, protection, care, assistance, society, companionship, comfort, guidance, counsel and advice in accordance with G.L, c. 229, §2 and that these damages be held by the Executor/Administrator Plaintiff as Trustee for the statutory beneficiaries;

g. Laura Allen and each child demands that they be provided with fair and reasonable funeral burial expenses incurred on behalf of the decedent in the amount of $30,000 pursuant to G.L. c. 229, §6A;

h. Enter judgment in favor of Plaintiffs for actual damages and for all other relief, in an amount to be proved at trial, as to which they may be entitled, for interest, attorneys' fees, expert fees and costs of this suit;

i. Award treble damages and/or punitive damages together with attorney fees and costs under 93A;

j. Award prejudgment and post judgment interest as provided by law; and

k. Enjoin the Defendants from selling their product in the Commonwealth without first eliminating, minimizing and warning of the danger presented; and

l. Award such further relief, as this Court deems necessary, just, and proper.

DEMAND FOR TRIAL BY JURY

The Plaintiffs hereby demand a jury trial as to all issues in this action.

Dated: May 31, 2006

Respectfully Submitted,
The Plaintiffs,
By their counsel

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CERTIFICATE OF SERVICE

I, Michael R. Hugo, certify that on this 29th day of October, 2007, I caused all counsel of record to be served the within THIRD AMENDED COMPLAINT , via the Electronic Court Filing system.

/S/ Michael R. Hugo

EXHIBIT B

UNITED STATES DISTRICT COURT
FOR THE
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY; And As ADMINISTRATRIX OF THE ESTATE OF DANIEL ALLEN; And AS NEXT FRIEND OF TAYLOR ALLEN AND DANIELLE ALLEN; And MARK ALLEN, Plaintiffs; v. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES; And SOUTHWEST RECREATIONAL INDUSTRIES, INC., d/b/a MARTIN SURFACING; Defendants.	CIVIL ACTION No.: 05-40048

RULE 26 EXPERT REPORT- L. CHRISTINE OLIVER, M.D.

I am writing with regard to the results of my medical evaluation of Coach Daniel Allen. My findings and opinions, and the bases for these opinions, are provided below. These are based upon my review of the following: 1) medical records; 2) a personal exposure and symptom diary kept by Mr. Allen; 3) Southwest Recreational Industries, Inc.'s Supplemental Responses to the Plaintiffs' Request for the Production of Documents; 4) Material Safety Data Sheets (MSDS) for products used during the installation of Versaturf '360' in the Field House of The College of the Holy Cross in Worcester, MA in late May/early June, 2001; 5) the Technician's Manual for the Installation of Versaturf '360'; 6) email correspondence between Mr. Allen and administrative personnel at Holy Cross College; 7) affidavits of co-workers of Mr. Allen and of one of the applicators of the Versaturf flooring system; 9) deposition testimony of a) Rod Paul, an employee and Projects Manager at Southwest Recreational Industries at the time of the installation of the floor, b) Scott Merrill, Director and former Assistant Director of the Physical Plant at Holy Cross College, and c) Mrs. Laura Allen, Mr. Allen's widow; 10) expert report; 11) observations at the time of a walk-through inspection of the Field House at Holy Cross College, including the gymnasium itself and the office of Coach Allen; and 12) floor and heating, ventilation, and air conditioning system (HVAC) plans for the Field House.

Medical records are from the UMass Memorial Medical Center (UMMC) in Worcester, MA and the offices of Drs. Richard A. Palken, Daniel A. Pollen, David A. Chad, Nicholas Smyrnios, Stephen J. Krinzman, Brian D. Busconi, and John V. Shufflebarger of UMMC; James A. Russell, DO of the Lahey Clinic in Burlington, MA; Harvard Pilgrim Health Care; and Sharon Home Health Care. Medical records cover the time period October 3, 1992 through May 11, 2004. Dated email and written correspondence cover the time period August 2, 2002 to August 12, 2003. Co-workers from whom affidavits were obtained are Robert J. Bradley, Paul T. Bachia, and Larry Napolitano; the Versaturf '360' applicator is Paul Crecelius. Affidavits were signed on May 18, May 19, May 10, and May 11 2007, respectively. Deposition testimony was taken of Mrs. Allen on March 13, 2007 in Boston, MA; of Mr. Paul, on April 11, 2007 in Baltimore, MD; and of Mr. Merrill, on June 14, 2007 in Boston. Expert report is from Marcia H. Ratner, PhD, Director and Neurologist and Neurotoxicologist, respectively, of the Environmental and Occupational Neurology Program and Department of Neurology at Boston University School of Medicine, dated June 14, 2007.

In addition, I have relied upon my own professional experience and publications in the medical and scientific literature. These include but are not limited to those provided at the end of this report. A copy of my current curriculum vitae has been provided.

I anticipate the review of an expert report by William Ewing, CIH, of Compass Environmental in Marietta, GA when it becomes available.

Medical History

Mr. Allen was in his usual state of good health until May, 2001. On or about May 22 of that year, the process of installing the Versaturf '360' polyurethane flooring system in the Field House at Holy Cross College was begun. Early in the course of the installation Mr. Allen, as described in his diary, was "overcome with the fumes" and "developed a severe headache, nausea with dizziness as well as disorientation." As the day went on, his symptoms became worse to the point that the room was spinning and he had to leave. The following day he returned to work, only to find that the fumes had not dissipated. Headache and nausea persisted.

Mr. Allen vacationed with his wife in Aruba from July 23-29. While on vacation he developed "severe diarrhea", treated with Ciprofloxacin. On August 3, 2001 he was seen by Dr. Palken, his primary care physician. The office note indicates diarrhea for eight days, and headache, dizziness, and "sweaty." On August 29, September 18, October 22, and October 23 Mr. Allen was seen by Dr. Palken or contacted his office because of persistent headache, dizziness, and nausea. On October 23, Dr. Palken notes headache, increasing in severity and frequency. He ordered a brain MRI/MRA and prescribed Neurontin. MRI/MRA on October 30 was within normal limits.

On November 15, 2001 Mr. Allen was evaluated by Dr. Pollen in the Headache Clinic of UMMC. A history was obtained of throbbing bilateral temporal or occipital

headaches that worsened during the course of the day and had been associated with vertigo and nausea for the three weeks preceding the visit. On an intake form completed by Mr. Allen at the time of that visit he noted both nocturnal and daytime calf cramps and muscle twitching. Neurologic examination by Dr. Pollen was normal. He concluded that Mr. Allen had headaches of "transform migraine", with related vertigo, as well as "restless leg syndrome." Neurontin was continued and the dose increased.

Mr. Allen notes in his diary that in September he developed muscle fasciculations as well, in his legs. He also notes at that time that "I did not mention anything to my doctor about the exposure because I didn't put it together that that was what caused my condition." In October headaches and dizziness persisted and at times made it difficult for him to function. During the fall of 2001 fasciculations in his lower extremities increased and spread to his arms and upper body. In his diary he writes "I basically dealt with it for a couple of more months."

Dr. Palken referred Mr. Allen to Dr. Chad, neurologist at UMMC, for evaluation of fasciculations. Mr. Allen obtained an earlier appointment with Dr. Russell, neurologist at the Lahey Clinic, and was seen by him on January 22, 2002. At that time, Mr. Allen was noted to be a 46 year old left-handed football coach at Holy Cross referred for assessment of fasciculations, with elevated creatine phosphokinase (CPK) at 511. History revealed onset of fasciculations in the thigh and right shoulder in approximately August, 2001. He also reported fatigue but denied functional impairment. There was no history of weight loss or symptoms of autonomic nervous system dysfunction. There was also no family history of motor neuron disease (MND). Medications were Zestril for hypertension, neurontin for headache, and aspirin for cardiovascular prophylaxis. Physical examination revealed diffuse fasciculations over the shoulders and thighs, primarily. Mr. Allen appeared anxious and blood pressure was elevated at 140/100. Left foot dorsiflexion was intact but dorsiflexion of the left great toe was markedly diminished at 4- (vs. 4+ on the right). Deep tendon reflexes were decreased in the right upper extremity compared to the left. Mr. Allen was unable to walk on his left heel. He was able to do single leg-toe rises bilaterally, better on the right than the left. Pin prick and vibration were decreased over the left great toe compared to the right. Grip strength was 104 lbs on the right and 127 lbs on the left. Dr. Russell's initial assessment was that Mr. Allen's presentation with fasciculations was unusual for MND; however, the widespread nature of the fasciculations, taken together with left foot drop and elevated CPK, were considered indicative of a pathologic process. Dr. Russell ordered nerve conduction and electromyographic (EMG) studies. The former were within normal limits. The latter showed "widespread fasciculations and findings of chronic denervation and reinervation."

On January 28, 2002 Mr. Allen was examined by Dr. Chad at UMMC. He reported to Dr. Chad the resurfacing of the floor of the Field House and the symptoms he experienced during that time. Physical examination by Dr. Chad revealed multisegmental fasciculations involving the muscles of the upper back, shoulder, upper arm, forearm, and thighs. No muscle atrophy was appreciated. Weakness of the left foot and toe extensors was described. Right biceps and brachioradialis reflexes were decreased and "brisk" for right triceps and leg reflexes. Heel walking was abnormal because of weakness of the left

foot. The remainder of the neurologic exam was normal. It was Dr. Chad's opinion that symptoms, physical findings and EMG results suggested MND. Lyme titer and 24-hour urine for heavy metals were ordered. Mr. Allen was given a prescription for Rilutek and advised to take vitamins C and E. Lumbar puncture was attempted on the following day without success and performed under fluoroscopic guidance on February 15. The cerebrospinal fluid (CSF) was clear, with normal protein, glucose, and cell count, and negative VDRL.

Mr. Allen was seen in follow-up by Dr. Russell on February 18, 2002. At that time he appeared healthy and had noted no change in symptoms. There was no evidence of bulbar involvement. Right grip strength was increased 12 lbs compared to January; and left grip, decreased by 1 lb. Lower extremity strength was normal, as was walking. It was Dr. Russell's conclusion that Mr. Allen had probable MND. He so counseled the Allen family. He prescribed quinine sulfate for muscle cramps and raised the question of Mr. Allen's participation in a study investigating the therapeutic utility of Celebrex. On February 22 Dr. Russell noted that the following test results were normal: Lyme screen; MRI of the cervical spine; 24-hour urine for arsenic, lead, and mercury; CBC; erythrocyte sedimentation rate; serum protein electrophoresis; CSF antiglycolipid antibody (GM1); and B12. Thyroid stimulating hormone was mildly elevated at 4.4.

In early March, 2002 Dr. Palken diagnosed reactive depression and prescribed Remeron. When next seen on August 2, Mr. Allen reported persistent "cramps" and a history of having received intravenous EDTA. Physical exam revealed "palpable and visible fasciculations" and lower extremity weakness of the dorsiflexor muscles. He noted that Mr. Allen could not walk on his heels and could barely walk on his toes. Bilateral clonus was noted. His assessment was amyotrophic lateral sclerosis (ALS). When next seen by Dr. Palken on October 2, 2002 Mr. Allen reported a tickle in his throat and dizziness and nausea when at work in the Field House, but not outside of the Field House. His legs were weak, the left greater than the right. He reported no upper body weakness. Medications were Synthroid, folic acid, calcium and magnesium, and vitamins E and C. Chest X-ray on that day was reportedly normal. Spirometry performed on October 4 was normal: FEV_1 (L) 4.54, 121% predicted; FVC (L) 4.99, 99% predicted; FEV_1/FVC 0.91; PEF (L/sec) 9.63, 104% predicted.

In the spring of 2003, Mr. Allen became wheelchair-bound because of inability to walk. In late December he was referred by Dr. Palken to Dr. Smyrnios of the UMMC Division of Pulmonary, Allergy, and Critical Care Medicine because of dyspnea. The dyspnea was noted by Dr. Smyrnios to be "manifested primarily by inability to generate an adequate voice because he does not get enough air." He further noted that Mr. Allen was able to stand with partial support for only three to four minutes. He was also unable to use his arms and had not been able to write since June. There was no history of prior respiratory tract illness or disease, and no history of tobacco use. He was able to eat, with occasional cough. Medications were amitriptyline, Klonopin, Benzphetamine, vitamins E and C, repoic acid, folic acid, and Probiotics. Physical examination revealed Mr. Allen to be "thin and debilitated", seated in a wheelchair. Tongue movements were normal and

there were no fasciculations. Lungs were clear. Fingers were contracted and he was not able to move his arms or legs. Pulse oximetry was normal at 98%.

On January 4, 2004 Mr. Allen was seen in follow-up by Dr. Smyrnios and lung function tests were obtained. Spirometry showed marked decreased in FEV_1 and FVC compared to October, 2002: FEV_1 (L) 1.18, 32% predicted; FVC (L) 1.40, 28% predicted; FEV_1/FVC 0.84. Total lung capacity was reduced at 50% predicted; single breath diffusing capacity for carbon monoxide (DLCO) was normal with correction for alveolar volume at 128% predicted. Maximal inspiratory and expiratory muscle forces were markedly reduced at 27 and 28 cm H_2O, respectively. Chest radiograph showed low lung volumes. Dr. Smyrnios concluded that Mr. Allen had neuromuscular disease consistent with ALS from a pulmonary standpoint. He noted "dramatic deterioration over the past 14 months", with respiratory failure being an imminent threat. Dr. Smyrnios prescribed BiPAP and cough in-exsufflator to assist Mr. Allen breathing. At that time Mr. Allen declined a feeding tube. Tracheotomy and mechanical ventilation were also discussed.

On April 13, 2004 Mr. Allen was examined by Dr. Joe Jabre and Marcia Ratner, PhD at the Boston University School of Medicine. Neurologic exam revealed generalized weakness of his upper and lower extremities to the point of his being wheelchair-bound, contractures of his hands and feet, atrophy and fasciculations of his tongue, absent deep tendon reflexes at the ankle and knee, positive Hoffman's, and mild loss of pinprick sensation in his lower extremities.

One week later on April 21 Mr. Allen was seen in follow-up by Dr. Smyrnios. By that time, Mr. Allen had developed trouble swallowing and eating and drinking. He was able to take only a few sips of liquid at a time. BiPAP was used only intermittently because the air was dry and the machine uncomfortable. Secretions were increased and the cough in-exsufflator ineffective in removing them from the chest. Physical exam revealed him to be in a wheelchair, frail-appearing and speaking in a soft voice. He had tachycardia attributed to dehydration. Dr. Smyrnios' assessment was ALS, rapidly deteriorating and without benefit from homeopathic remedies. In his opinion, a feeding tube was needed. He prescribed intravenous hydration at home and nasal pillows and humidification for the BiPAP machine. Sharon Home Health Care saw Mr. Allen on the same day. On May 4, 2004 Mr. Allen was admitted to UMMC for hydration and placement of a gastric feeding tube (PEG). Arterial blood gases on admission were consistent with respiratory failure: pH 7.36, pO_2 68 mmHg, pCO_2 71 mmHg. PEG placement was performed at the bedside, as the family did not want Mr. Allen intubated and placed on a ventilator.

Mr. Allen was discharged in stable condition on May 7, 2004 to be followed at home by the Visiting Nurse Association, with additional care from home health aides. He died nine days later on May 16. Records of the events immediately surrounding his death are not available. The death certificate gives as cause of death "neuromuscular degeneration." Postmortem examination was not performed.

Past medical history reveals hypertension and bifrontal headaches. In 1992 he tore his rotator cuff on the left, with subsequent acromioclavicular joint arthritis and mild

impingement. He was followed for this problem by Dr. Busconi, and in 2000 had arthroscopy with debridement and subacromial decompression. Other surgical procedures included appendectomy, hand surgery, hernia repair, and vasectomy. On May 3, 2001 he underwent colonoscopy because of blood in his stool; findings were normal and blood was attributed to daily aspirin. On May 14, 2001 he underwent removal of skin tags on his back and a sebaceous cyst on his scalp. On May 22, 2001 he was seen by a nutritionist with regard to implementation of a weight loss regimen. Mr. Allen was active throughout his adult life. He did not use tobacco; alcohol consumption was limited to a couple of beers per week. His only known drug allergy was to Paxil. Family history reveals that his mother smoked cigarettes and died of lung cancer at age 58 or 59. Mr. Allen never knew his father. Mrs. Allen testified (p.19) that to her knowledge his father lived to at least 80 years of age, with diabetes mellitus being his only known disease. He had one brother, in good health with high blood pressure. One half-brother and four half-sisters were alive and well in 2004, with the exception of hypertension. Mr. Allen has three children, ages 19, 14, and 12 at the time of his death. One of his children has Hashimoto's thyroiditis. At the time of his death, Mr. And Mrs. Allen had been married for 27 years. She is a registered nurse.

Occupational and Exposure History

Occupational history reveals that Mr. Allen graduated from Purcell High School in Cincinnati, OH in 1974. He attended Hanover College in Indiana and then obtained a Master's degree in school administration from the University of Dayton. He worked as a graduate assistant to the football team there for one year after graduation and then took a job at Mariemont High School in Cincinnati. He taught science and coached football and track from approximately 1979 to 1981. From 1981 to 1982 he worked as assistant football coach at Hanover College. In 1982 Mr. Allen went to work for The College of the Holy Cross as assistant football coach. He held this position until 1990 when he went to work for Boston University as head coach for the football team. In 1995 when Boston University abolished their football program, he went back to Holy Cross as head football coach. He held this position until November, 2003 when he was terminated because of his MND and its attendant disability.

Southwest Recreational Industries, Inc.'s Responses to the Plaintiffs' Request for the Production of Documents reveal that in the spring of 2001 The College of the Holy Cross contracted with Southwest Recreational Industries (D/B/A Martin Surfacing) to resurface the flooring in the Field House during the time period May 21 to June 8, 2001. According to the terms of the agreement, 17,000 sq.ft. of flooring was to be resurfaced with Versaturf '360' – a 100% mercury-free polyurethane athletic surface. The installation included gamelines and coatings as they presently existed.

Specifications for projects such as the one carried out in the Field House at Holy Cross College call for the removal and disposal of the top 1/16 inch of floor surface, to be replaced by a 1/8 inch Versaturf '360'surface. According to testimony by Rod Paul, the installation process calls for the deep cleaning or abraiding of the existing surface with a drum sander. Then a primer is spray-applied for adhesion. After the primer has dried, the

polyurethane floor is poured. The polyurethane is prepared by machine-mixing Parts A and B and transferring them by a hose into 5-gallon buckets. It is poured from the buckets over the entire floor, raked out, and allowed to dry. Finally a coating is sprayed on and the gamelines painted. The drying of both primer and polyurethane are affected by heat and humidity – with higher temperature and relative humidity retarding drying. Mr. Paul testified (pp.32, 33) that to keep humidity at the proper level "…. if you haven't already done so, to make sure that the … either the heat or the air conditioning is on in the building to reduce the relative humidity." The Technician's Manual for the Installation of Versaturf '360' specifies (Section 8, 4) that the technician should (a) "make sure the HVAC system is operational and running before you begin" and (b) "if it is on a timer, it should be by-passed to keep the heat or AC running." Section 24 states "Each time you run the machine, it must be flushed with trichloroethane immediately after."

Mr. Merrill testified that an HVAC system installed in the Field House in approximately 1992 as part of a larger renovation project serviced the Athletic Department offices on the first and second floors of the Field House, but not the gymnasium itself (pp.26, 27; lines 4-15 and 14-21, respectively). He also testified (p.83, lines 4-8) that the air in the gymnasium is "not conditioned air", i.e., it is neither heated nor cooled/dehumidified.

Specifically with regard to the installation of Versaturf '360', Mr. Crecelius described the following: 1) sanding the existing floor with a Ryder Sander to "rough up" the floor, 2) cleaning and vacuuming the floor, 3) spraying the floor with a primer, 4) applying a resin coating approximately 1/8 inch thick to the floor, 5) spray painting the floor to the desired color, and 6) laying out the gamelines and painting them by roller. He noted that the applicators wore a "full-face organic filter respirator" during the process. Mr. Crecelius described taping the doors leading into the lobby area with plastic and using a large industrial fan to blow the fumes out of the work area after the floor was dry. He indicated in his affidavit that "If the field house had air conditioning and/or heat, it would not be turned on" while the floor was drying.

Part G of the Responses to the Plaintiffs' Request was "The Material Safety Data Sheet (MSDS) for each product used for the Project." Part G consists of MSDSs for the following products: Versaturf '360' Part A, manufactured by Southwest Recreational Industries (MSDS dated April 14, 1999); Mondur 448 Part B, manufactured by Bayer Corporation (MSDS dated January 1, 1996); Richmold 303-0002, manufactured by Carpenter Company Chemical Systems Division (MSDS dated October 29, 1997); Futura Tech 506A Clear 1:1, manufactured by Futura Coatings, Inc. (MSDS dated February 4, 1997); Futura Tech 506B 1:1 (MSDS dated February 4, 1997); D-186 Primer, manufactured by Development Associates, Inc. (MSDS dated December 12, 1994); Futura Tech 8553B, manufactured by Futura Coatings, Inc. (MSDS dated February 12, 1997); Futura Tech 8553A and 8563A (MSDSs dated December 12, 1996); and Futura Tech 8563B Red Line Paint (MSDS dated October 27, 1997).

Solvents contained in these products include polyoxy propyleneglycol 65% by weight (Versaturf '360'); aromatic hydrocarbon NOS 45-61%, acetone solvent 0-14% (Futura Tech 506A Clear); toluene 5-20%, ethanol 40-70%, 2-ethylhexanol 1-10%, and diacetone alcohol 1-10% (D-186 Primer); aromatic hydrocarbon NOS 10-26%, glycol ether acetate 10-26% (Futura Tach 8553B All Colors); and aromatic hydrocarbon NOS 27-43% (Futura Tech 8553A). Trichloroethane was used to clean the machines after each application. Versaturf '360' also contained methlene bis (phenylisocyanate) (MDI); and Mondur 448, higher oligomers of MDI and 2,2, 2,4, and 4,4 diphenylmethane diisocyanate.

In his diary, Mr. Allen described being "overcome" with fumes during the installation of Versaturf '360' in the Field House. He further described persistence of fumes during the period of the resurfacing. Mr. Robert (Bob) Bradley was Assistant Football Coach in the spring and summer of 2001. He testified in his affidavit that his office was about ten yards from Coach Allen's office, on the same floor. He estimated that the resurfacing was carried out about ten yards below his and Coach Allen's offices. He recalled that the weather during the period of the floor installation was hot and humid and that the air conditioning was on; so that the windows would have been closed. Mr. Bradley testified that "During the re-surfacing work, I smelled and felt the effect of the fumes from the chemicals being used by the workers; the fumes were noxious; I felt dizzy and suffered headaches throughout this period." He noted that before the resurfacing began "Coach Allen appeared perfectly healthy to me." At the time, the football coaches and their staff were preparing for the annual Football Camp, scheduled to begin just after completion of the floor installation. Coach Allen let his staff and assistants leave early each day because of the chemical exposures; but he stayed to finish preparations for the Camp.

Mr. Paul Bachia was the Running Backs Coach at this time. He testified in his affidavit that his office was directly across from Coach Allen's office. He concurred with Mr. Bradley that the resurfacing was carried out about ten yards below the offices on the second floor. As he recalled, the work took approximately two weeks. Mr. Bachia describes smelling and feeling "the effect of the fumes from the chemicals being used by the workers: I felt a burning sensation in my eyes and, when I breathed deeply, I felt a burning sensation in my throat." He also described feeling lightheaded and noted that Coach Allen was lightheaded and nauseous. Mr. Napolitano was the coordinator of athletic media relations at Holy Cross College in May, 2001. His office was on the ground floor of the Field House. He testified in his affidavit that the workers were "right outside my office door at one point. They were directly underneath Coach Allen's office." He reported pounding headaches and nausea during the period of the resurfacing. Headaches were directly linked to his presence in the Field House. He noted "The smell just permeated everything and with the heat rising to the top of the building it was just worse and worse every day. I could tell it was worse where Coach Allen was located, when I would go up and see him. At least I could open my windows to the outside. He could not open his windows."

According to Mr. Merrill's testimony (p.76, lines 9-11), air quality testing was carried out in the gymnasium on August 15, 2002, over a year after the installation of the

flooring system. An email from Mr. William Conley to Mr. Allen dated September 20, 2002 reports the results of air quality testing done in the Field House. Mr. Merrill's testimony (p.76, lines 9-11) indicates that the testing was carried out on August 15, 2002. Results as described in the email revealed elevated levels of volatile organic compounds (VOCs), attributed by Mr. Conley to recent painting in the building, with propylene glycol and methyl ether acetate being the predominant chemicals identified. Also noted were "very high" levels of airborne particulates $\geq$ 0.3 microns in diameter. Levels of MDI were detectable, although in concentrations less than 0.001 parts per million (ppm). The scope and actual results of the air quality testing are not available.

Assessment

In summary, Mr. Allen had a history of occupational exposure to solvent vapors and aerosols at the time of the resurfacing of the gymnasium floor in the Field House at The College of the Holy Cross in Worcester, MA. The exposure occurred in late May/early June, 2001. At the time he was working as Head Football Coach at the College, a position he had held since 1995. His office was on the second floor of the Field House, about 10 yards from the gymnasium. The resurfacing took approximately seven to ten days; although the actual duration of the project is not specified in any of the materials available for review. Mr. Allen estimated a period closer to 14 to 21 days; Mr. Bradley, about two weeks.

In his personal diary, Mr. Allen described being "overcome with the fumes" from the floor resurfacing. Symptoms included headache, dizziness, nausea, and disorientation. Despite these symptoms, he returned to work on a daily basis during this time, as he was preparing for the College's annual football camp. Co-workers in offices proximate to Mr. Allen's reported similar symptoms – headache, dizziness, lightheadedness. When he returned from a July vacation, Mr. Allen's symptoms returned and persisted. In September he developed, in addition, fasciculations in his lower extremities. Subsequently fasciculations spread to his upper extremities and trunk. In October headache increased in frequency and severity.

In January, 2002 Mr. Allen was evaluated by two neurologists – Dr. Chad at UMMC and Dr. Russell at the Lahey Clinic. Based on medical history and physical and laboratory findings, both diagnosed ALS. Mr. Allen's course was relentlessly progressive and he died of his disease on May 16, 2004, approximately 16 months after diagnosis.

In my opinion, Mr. Allen had ALS and died as a result of his disease. Mr. Allen was diagnosed with ALS by his treating physicians in January/February, 2002. Medical records and death certificate indicate that he died less than two years later as a consequence of his disease.

ALS is a degenerative disease of the nervous system affecting the motor neurons, hence its classification as a MND.[1] Males are more commonly affected than females. Age at onset is generally greater than 50 years; incidence increases with increasing age. Approximately 5% are familial, inherited as an autosomal dominant trait. The remainder

are classified as "sporadic", without clearly demonstrated cause. Presenting symptoms are variable and include fasciculations of the upper and/or lower extremities, weakness of the leg and foot drop, and loss of fine finger movements. As the disease progresses, the trunk and respiratory muscles are affected, as are the muscles of the tongue, pharynx, and larynx. Approximately 50% of those affected die within three years; 90%, within six years.

Pathologic examination of the spinal cord and lower brain stem reveals loss of motor neurons in ALS. In some familial cases, mutation of a gene that codes for Cu-Zn superoxide dismutase (SOD) has been described. The result is a 20 to 50 percent decrease in SOD enzyme activity, causing an excess of free radicals that is associated with degeneration of neurons. Additionally, SOD enzyme deficiency is thought to be associated with increase in glutamate concentrations in the extracellular space, with resulting increase in glutaminergic excitotoxicity and motor neuron degeneration. Additional enzymatic and biochemical mechanisms have been proposed as pathogenic in ALS; these are described in detail by Dr. Ratner.[2]

In Mr. Allen's case, initial symptoms were fasciculations in the leg with weakness and foot drop. Symptoms spread to his arms and upper trunk. He developed decrease in respiratory muscle force as a result of muscle weakness, causing severe impairment in lung function. Ultimately muscles of his pharynx and tongue were affected, resulting in difficulty ingesting food and liquid.

In my opinion, Mr. Allen had sporadic ALS. History taken of Mr. Allen himself as reflected in the medical record and deposition testimony of his widow reveal no family history of ALS. As the disease is inherited as an autosomal dominant trait, the absence of family history makes familial ALS most unlikely.

In my opinion, the time of onset and rate of progression of ALS in Mr. Allen's case were causally related to his exposure to solvent vapors and aerosols during the course of the installation of the Versaturf '360' flooring system in the Field House of The College of the Holy Cross.

In late May/early June, 2001 Mr. Allen was working in his office on the second floor at the west end of the Field House. He reported in his diary that he "became overcome with the fumes." At the time, the installation of the Versaturf '360' in the gymnasium had begun. Solvents found in the chemical products used in the installation included toluene, aromatic hydrocarbons not specifically identified because of trade secret, ethanol, 2-ethylhexanol, diacetone alcohol, acetone, glycol ether acetate, and trichloroethane. The primer and coatings were spray-applied, creating an aerosol and enhancing availability for inhalation. Solvent vapors were released into the air from the primer, the polyurethane flooring system, and the coatings as each dried.

The symptoms which Mr. Allen and his colleagues developed during this time period are consistent with neurotoxic effects of solvents – namely headache, dizziness, nausea, and disorientation.[3,4] The occurrence of these symptoms and their persistence suggest that exposures were at or above the permissible exposure limit (PEL) established by the

Occupational Safety and Health Administration (OSHA) of 200 ppm, established as an eight hour time-weighted average for workers in an industrial setting.[5] Exposure of human subjects to toluene at 600 ppm for eight hours has been associated with headache, dizziness, nausea, dilated pupils, and euphoria; symptoms were enhanced with exposure at 800 ppm.[4] Thus, the nature of Mr. Allen's symptoms and the distinct temporal relationship between their onset and persistence and the installation of the Versaturf '360' flooring system are consistent with and make likely a causal association.

These are two of the cornerstones to the determination of exposure-related disease in occupational medicine: consistency of symptoms and clinical manifestations with what would be expected to occur in association with a given exposure and a temporal association between onset/worsening of symptoms and that exposure. Another cornerstone is the use of differential diagnosis to exclude other possible causes. The application of the differential diagnostic method to the review of Mr. Allen's medical records, Mrs. Allen's deposition testimony, and the affidavits of co-workers who knew Mr. Allen well reveals that he was active and healthy prior to the exposures incurred in the early summer of 2001. There is no family history of ALS; so that he did not have familial ALS. Other putative causes include exposure to pesticides and "agricultural chemicals" (which contain solvents), sixty hertz magnetic fields, and welding fume.[6,7] There is no evidence that Mr. Allen had exposure to these agents.

Dr. Ratner in her report has provided ample evidence of the motor neuron toxicity of solvents generally and toluene specifically, with an emphasis on enzymatic and biochemical mechanisms.[2] She has concluded "with a reasonable degree of medical certainty" that Mr. Allen's exposure to the chemicals used in the resurfacing of the Field House gymnasium floor hastened the onset of Mr. Allen's ALS and his consequent demise.

Epidemiologic evidence also supports a causal association between exposure to solvents and the development of ALS. Solvents are well known toxicants for the central nervous system and the peripheral nervous system.[8] Hawkes et al in 1989 was one of the first to raise the question of a causal relationship between occupational exposure to solvents and MND, having observed that of 164 deaths among leather industry workers, 33 (20.12%) were due to MND.[9] The authors suggest that "a direct neurotoxic action effect" of solvents on the motor neurons "deserves most consideration" (p.75). Shortly after the publication of the article by Hawkes, Chio et al in a Letter to the Editor presented data on occurrence of MND among workers in a variety of trades exposed to solvents and glues.[10] These included typesetters, painters, carpenters, tanners, and workers in the rubber production industry. Although failing to achieve statistical significance because of small numbers, for each odds ratios were greater than 1 at 2.4, 2.8, 5.1, 3.7, and 1.7, respectively.

In a case-control study of 103 patients with MND in Scotland, and 103 referents from the community matched on age and gender, Chancellor et al observed a significant increase in risk for exposure to solvents/chemicals among cases compared to the reference group (OR = 3.3, 95% confidence interval (CI) 1.3-10).[11] A case-control study carried out in the northwest region of England examined risk factors for MND, matching each of 128 cases

with two controls based on gender, age, and geographic area of residence.[12] Exposure to fumes and dust was significantly associated with MND (RR = 2.46, 95% CI 1.47-4.09).

Comparing 174 newly diagnosed cases of ALS with 348 matched controls, McGuire et al observed a two fold increase in risk with occupational exposure to alcohols or ketones (OR = 2.0, 95% CI 1.0-4.0) and a 90% increase in risk with exposure to cleaning solvents or degreasers (OR = 1.9, 95% CI 1.1-3.3).[6] For alcohols and ketones, risk was greater in men than in women (OR = 2.6, 95% CI 1.1-6.1 vs. OR = 1.2, 95% CI 0.4-3.7). Exposure was assessed on the basis of job history by a panel of four industrial hygienists blinded as to disease status and self-reported exposures.

Using death certificate data from the National Occupational Mortality Surveillance System, Park et al calculated mortality odds ratios (MOR) for several neurodegenerative diseases, including MND.[7] Usual occupation and business or industry were obtained from the death certificates. Comparison group consisted of all deaths without mention of neurologic disease on the death certificate. Exposure to solvents and benzene was assessed using a standardized job-exposure matrix, with further classification of probability and intensity of exposure: none, low, medium, high. The total number of deaths was 2,614,346; 112,805 were due to neurodegenerative disease. Of these, 6,347 were attributable to MND. A significant elevation of MOR for MND was observed for occupational exposure to solvents (MOR = 1.16, 95% CI 1.01-1.34). Risk factors for sporadic ALS (SALS) were examined in a case-control study in Australia, comparing 179 ALS patients with controls without known neurologic disease.[13] Exposures were self-reported using a structured questionnaire. Significant associations were observed for occupational exposure to solvents/chemicals for the total group (OR = 1.92, 95% CI 1.26-2.93, p=0.003) and for males (OR = 1.85, 95% CI 1.12-3.04, p=0.023) and females (OR = 2.57, 95% CI 1.05-6.31, p=0.066) independently. The authors concluded "that occupational exposure to solvents/chemicals is an important risk factor for SALS in the Australian population."

In a prospective population-based study, Chio et al examined the predictive value of age at onset and symptom progression for survival time in ALS.[14] The cohort consisted of 221 patients with ALS enrolled in the study in 1995 and 1996 and monitored for a little more than five years using a standardized evaluation form. The median age-at-onset was 62.8 years (standard deviation (SD) 11.2 yrs). The median survival time from age at onset was 915 days (95% CI 790-1065). Age at onset was significantly associated with survival time (p=0.007). Age was noted to be "probably the most consistent factor related to outcome" (p.101), with older age at onset being associated with more rapid progression. Each of the six patients with symptom onset at less than 40 years of age was alive at the end of the follow-up period. Three and five-year survival from age at onset for the group as a whole was 40.5% (SE = 3.5%) and 24.7% (SE = 3.1%, respectively. Mr. Allen was 45 years of age at the time of onset of his disease. His subsequent survival time was approximately 2.7 years.

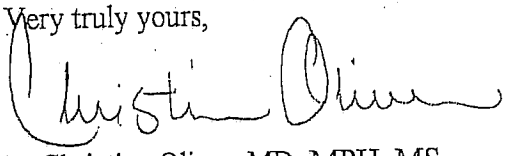
Thus in vitro data from toxicological studies, in vivo data from animal studies, and epidemiologic data from studies in human populations in a number of different countries

all support a causal association between solvent exposure and the development and/or exacerbation of MND in the form of sporadic ALS.

In my opinion, Southwest Recreational Industries, Inc., d/b/a Martin Surfacing, was negligent a) in its failure to warn Mr. Allen and other athletic staff of the potential toxicity of the chemicals used in the installation of the Versaturf '360' polyurethane flooring system and b) in its failure to ensure that these personnel were either adequately protected or vacated from the Field House during the installation process. This opinion is based upon information contained in Mr. Allen's diary and the affidavits of three colleagues working in the building at the time, as well as the known toxicity of the chemicals used in the floor resurfacing. Chemicals contained in the products used include not only solvents with known neurotoxicity, hepatotoxicity, and renal toxicity, but also diisocyanates with well-documented and potentially fatal respiratory toxicity as a result of irritant and sensitizing properties.[15]

I hold all of the opinions expressed in this report to a reasonable degree of medical certainty. I reserve the right to further supplement this report and respond to the reports submitted by the defense.

Very truly yours,



L. Christine Oliver, MD, MPH, MS

EXHIBIT C

TOWN OF WESTBOROUGH

Commonwealth of Massachusetts

I, Nancy J. Yendriga the undersigned hereby certify, that I hold the Office of Town Clerk of the Town of Westborough, in the County of Worcester, and Commonwealth of Massachusetts; that the Records of Births, Marriages and Deaths are in my custody and that the following is a true copy from the records, as certified by me.

TIONS ON REVERSE SIDE)
FOR USE BY PHYSICIANS AND EDICAL EXAMINERS

The Commonwealth of Massachusetts
STANDARD CERTIFICATE OF DEATH
REGISTRY OF VITAL RECORDS AND STATISTICS

REGISTERED NUMBER | STATE USE ONLY

DECEDENT

DECEDENT - NAME (1) First	Middle	Last	SEX (2)	DATE OF DEATH (Mo., Day, Yr.) (3)
Daniel	L	Allen	Male	May 16, 2004

PLACE OF DEATH (City/Town) (4a)	COUNTY OF DEATH (4b)	HOSPITAL OR OTHER INSTITUTION - Name (If not in either, give street and number) (4c)
Westborough	Worcester	2 Sawmill Drive

PLACE OF DEATH (Check only one): HOSPITAL: ☐ Inpatient ☐ ER/Outpatient ☐ DOA (5) | OTHER: ☐ Nursing Home ☒ Residence ☐ Other (Specify) (6)

SOCIAL SECURITY NUMBER (8): 275-58-3661

IF US WAR VETERAN SPECIFY WAR (7):

WAS DECEDENT OF HISPANIC ORIGIN? (If yes, Specify Puerto Rican, Dominican, Cuban, etc.) (8a): ☒ NO ☐ YES

RACE (e.g. White, Black, American Indian, etc.) (Specify) (8b): White

DECEDENT'S EDUCATION (Highest Grade Completed) (9): Elementary Sec (0-12): — College (1-4, 5+): 5+

AGE - Last Birthday (Yrs.) (10a)	UNDER 1 YEAR MOS. (b)	DAYS (c)	UNDER 1 DAY HOURS	MINS	DATE OF BIRTH (Mo., Day, Yr.) (10d)	BIRTHPLACE (City and State or Foreign Country) (11)
48					Dec 7, 1955	Cincinnati, Ohio

MARRIED, NEVER MARRIED, WIDOWED OR DIVORCED (12)	LAST SPOUSE (If wife, give maiden name) (13)	USUAL OCCUPATION (Prior to Retired) (14a)	KIND OF BUSINESS OR INDUSTRY (14b)
Married	Laura A Miller	Head Football Coach	College

RESIDENCE - NO. & ST., CITY/TOWN, COUNTY, STATE/COUNTRY (15a): 2 Sawmill Drive, Westborough, Worcester, Massachusetts

ZIP CODE (15b): 01581

FATHER - FULL NAME (16)	STATE OF BIRTH (If not in US, name country) (17)	MOTHER - NAME (GIVEN) (MAIDEN) (18)	STATE OF BIRTH (If not in the US, name country) (19)
Unknown	Unknown	Dolores Binkley	Ohio

INFORMANT

INFORMANT'S NAME (20)	MAILING ADDRESS - NO. & ST., CITY/TOWN, STATE, ZIP CODE (21)	RELATIONSHIP (22)
Laura A Allen	2 Sawmill Dr., Westborough, MA 01581	Wife

DISPOSITION

METHOD OF IMMEDIATE DISPOSITION (23)	FUNERAL SERVICE LICENSEE OR OTHER DESIGNEE (24)	LICENSE # (25)
☒ BURIAL ☐ CREMATION ☐ ENTOMBMENT ☒ REMOVAL FROM STATE ☐ DONATION ☐ OTH. SPEC.	Kevin L Mercadante	5985

PLACE OF DISPOSITION (Name of Cemetery, Crematory or other) (26a)	LOCATION (City/Town, State) (26b)
Rest Haven Memorial Park	Cincinnati, Ohio

DATE OF DISPOSITION (Mo., Day, Yr.) (27)	NAME AND ADDRESS OF FACILITY OR OTHER DESIGNEE (26c)
May 24, 2004	Mercadante Funeral Hm 370 Plantation St Worc., MA 01605

CERTIFIER

29 PART I - Enter the diseases, injuries, or complications that caused the death. Do not use only the mode of dying, such as cardiac or respiratory arrest, shock or heart failure. List only one cause on each line (a through d) PRINT OR TYPE LEGIBLY.

		Approximate Interval Between Onset and Death
IMMEDIATE CAUSE (Final disease or condition resulting in death) a.	Neuromuscular degeneration DUE TO (OR AS A CONSEQUENCE OF)	3 yrs
Sequentially list conditions, if any, leading to immediate cause. Enter UNDERLYING CAUSE (disease or injury that initiated events resulting in death) LAST b.	DUE TO (OR AS A CONSEQUENCE OF)	
c.	DUE TO (OR AS A CONSEQUENCE OF)	
d.		

PART II - Other significant conditions contributing to death but not resulting in underlying cause given in Part I. (30)

WAS AUTOPSY PERFORMED? (Yes or No) (31)	WERE AUTOPSY FINDINGS AVAILABLE PRIOR TO COMPLETION OF CAUSE OF DEATH? (Yes or No) (32)
NO	

MED. EXAM. NOTIFIED? (Yes or No) (33)	MANNER OF DEATH (34)	DATE OF INJURY (Mo., Day, Yr.) (35a)	TIME OF INJURY (35b)	INJURY AT WORK (Yes or No) (35c)
YES	☒ NATURAL ☐ HOMICIDE ☐ COULD NOT BE DETERMINED ☐ ACCIDENT ☐ SUICIDE ☐ PENDING INVESTIGATION			

DESCRIBE HOW INJURY OCCURRED (35d)	PLACE OF INJURY (At home, farm, street, factory, office bldg., etc.) Specify (35e)	LOCATION (No. & St., City/Town, State) (35f)

To be Completed by CERTIFYING PHYSICIAN ONLY

36a To the best of my knowledge, death occurred at the time, date, and place and due to the cause(s) stated. (Signature and Title)

DATE SIGNED (Mo., Day, Yr.) (36b)	HOUR OF DEATH (36c)
May 19 2004	1:30 P M

NAME OF ATTENDING PHYSICIAN IF NOT CERTIFIER (36d): Richard Pelken

To be Completed by MEDICAL EXAMINER ONLY

37a On the basis of examination and/or investigation in my opinion death occurred at the time, date, and place and due to the cause(s) stated. (Signature and Title)

DATE SIGNED (Mo., Day, Yr.) (37b)	HOUR OF DEATH (37c) M

PRONOUNCED DEAD (Mo., Day, Yr.) (37d)	PRONOUNCED DEAD (Hr) (37e) M

NAME AND ADDRESS OF CERTIFYING PHYSICIAN OR MEDICAL EXAMINER (Type or Print) (38): Richard Pelken 55 Lamb Ave N. Worcester MA 01605

LICENSE NO. OF CERTIFIER (39): 73003

WAS THERE A PRONOUNCEMENT? FORM (Yes or No) (40a)	IF YES, DATE PRONOUNCED (40b)	IF YES, TIME PRONOUNCED (40c) M	NAME OF PRONOUNCER (40d)	TITLE ☐ R.N. ☐ P.A.
NO				

DATE BURIAL PERMIT ISSUED (41)	RECEIVED IN THE CITY/TOWN OF	DATE OF RECORD
May 19 2004	Westborough	MAY 19 2004
SIGNATURE-BD. OF HEALTH AGENT: Paul R. McNulty	CLERK'S SIGNATURE (42): Kendra L Hurd	(43)

ANENT
INK ONLY

ement of Death
102) on File: ☐

Witness my hand and the Seal of the Town of Westborough this 19th day of May 2004.

Nancy J. Yendriga
TOWN CLERK

HC02242

EXHIBIT D

A. Overview of My "General" Causation Opinions

Most of this report delves into a good amount of scientific, pharmacological, and toxicological terminology and principles, which can be confusing or complicated for lay readers, but I have endeavored to explain my scientific bases as accurately and completely as possible. I therefore offer in this section, a more digestible summary of the underlying basis for my General Causation opinion, that the chemicals to which Dan Allen was exposed (and mostly I examine the chemical Toluene) were capable of hastening the onset of his ALS. It is really quite logical:

1. While science does not know what causes ALS, science does understand, and it is generally accepted as to how ALS occurs; that is, we do understand the neuropathology and the mechanisms by which neurodegeneration occurs, and I have described these mechanisms below.

2. The chemicals to which Dan Allen was exposed, and in particular Toluene, are known and generally accepted neurotoxicants; that is, they are toxic to, and can kill, human neurons.

3. Science also knows the mechanisms by which Toluene acts as a neurotoxicant, and this knowledge is also generally accepted; I have described these mechanisms below.

4. The mechanisms by which neurodegeneration occurs in ALS are exactly the same mechanisms by which Toluene acts upon neurons.

5. Scientific logic therefore dictates that Toluene is capable of altering or hastening subclinical and clinical course of ALS since the interaction of the toxic effects of toluene with the neuropathological mechanisms implicated in ALS will result in an additive effect.

6. We know that Dan Allen was exposed to sufficient levels of Toluene to succumb to its neurotoxic effects, because we know he presented with neurologic symptoms (headaches, dizziness) in exquisite temporal association with his exposure. I will demonstrate later in this document that the levels of exposure associated with the symptoms Dan Allen experienced were in excess of the current federal government Permissible Exposure Limit (PEL) of 200 parts per million (ppm) (see 29 CFR 1910.1000). We do not need to know a more specific level of exposure in order to make the causal inference here.

7. While few studies have looked at age at onset of ALS among subjects exposed to chemicals, many researchers have looked for chemicals that can slow the disease. The NINDS (National Institute of Neurological Disorders and Stroke) recognizes that the clinical course of the disease can be slowed by certain chemicals. "No cure has yet been found for ALS. However, the FDA has approved the first drug

treatment for the disease *riluzole*. Riluzole is believed to reduce damage to motor neurons and prolongs survival by several months, mainly in those with difficulty swallowing". [NINDS ALS information webpage; Miller RG *et al* 2005] *Riluzole, is a putative glutamate release blocker* that has modest benefit in extending survival, and is the only medication approved by the FDA for the treatment of ALS. [PDR, 2005, pp 744-746].

8. If a chemical can be used as a pharmaceutical to extend survival in ALS, can exposure to a chemical also curtail survival (or in order words, hasten onset of ALS)? To answer this question we will identify below putative points of interaction between the chemicals to which Mr. Allen was exposed in his workplace and the mechanisms of neurodegeneration implicated in ALS.

9. For example, if oxidative stress is implicated in ALS and Mr. Allen was exposed to a chemical that increases oxidative stress, then we have identified a putative point of interaction. Likewise, if increased glutamatergic neurotransmission is implicated in ALS and Mr. Allen was exposed to a chemical that increases glutamatergic neurotransmission, then we have identified another putative point of interaction.

10. In fact, review of the literature on ALS and the Material Safety Data Sheets of the chemicals used by Martin Surfacing to perform the floor re-surfacing at issue, clearly demonstrates that these were two of the ways in which the exposures that occurred during the floor refinishing process interacted with the latent disease from which Mr. Allen eventually died.

11. I will therefore present herein peer-reviewed scientific data supporting the conclusion that Mr. Allen's exposure to Toluene and other compounds used in the floor refinishing process at Holy Cross unmasked his latent ALS and was at least a substantial contributing factor to the progression of his disease.

My qualifications, the generally accepted method I followed in reaching this conclusion, and all the scientific bases upon which I rely in making these opinions, now follow.

B. My Qualifications

1. My professional education, experience and training have created a unique combination of clinical, academic and laboratory-based expertise in the very subject matter at issue in this legal case: assessing the causal role of an exposure to neurotoxic chemicals to the onset of a neurodegenerative disease. There are few scientists in the country with this clinical/academic/bench-science background. A copy of my CV is appended; and summarized as follows:

2. In 2004, I earned my Ph.D. from Boston University School of Medicine's Behavioral Neurosciences Program. I trained and worked directly with Robert

Feldman, M.D., generally considered one of, if not the world's foremost experts in neurotoxicology. From 1998-2004, I was the Senior Toxicologist and Project Manager working in conjunction with Dr. Feldman under the Department of Neurology's Environmental and Occupational Neurology Program. Our work resulted in several articles, textbook chapters and other professional writings, most of which are peer-reviewed, on the subject of neurotoxicology and neurodegenerative disorders. I am the co-author of those writings. Today, I remain the Senior Toxicologist for the Environmental and Occupational Neurology Program at the Boston University School of Medicine.

3. Between 2004 and 2007, I conducted and completed a post-doctoral fellowship supported by an NIH training grant in Aging in the Laboratory of Molecular Neurobiology within the Department of Pharmacology and Experimental Therapeutics at the Boston University School of Medicine. I focus my work in the lab in assessing the *in vivo* effects of novel chemicals, which may be developed into new drugs to address neurological and psychiatric disorders including neurodegenerative diseases. In that capacity, I have become an expert in the toxicological and pharmacological methods used by academic and industrial researchers to assess the ability of chemicals to alter the course of neurological disease.

4. Since 2004, I have been a research associate in the Department of Pharmacology and Experimental Therapeutics. In that regard, I am well studied and experienced in: (a) the scientific method for research; (b) biostatistics and epidemiology; the ability to understand and apply the results of scientific studies to consideration of causal assessment; and (c) assessing the quality of scientific studies.

5. Since 1998, I have been a research associate in the Department of Neurology at the Boston University School of Medicine. In that role, I have worked as a clinical research scientist evaluating patients with neurological conditions, including neurodegenerative disease such as ALS. I have worked closely with Dr. Joseph Jabre, the former chair of neurology at the VA Hospital and a faculty member at the School of Medicine at Boston University. As a research associate, I have become well-versed and experienced in the diagnosis and treatment of patients with neurodegenerative disorders. I am fully competent in performing clinical evaluations of such patients.

6. In recognition of my cross-over background in clinical neurology, pharmacology and expertise in neurotoxicology, I have been invited to lecture classes at the Boston University School of Medicine's Departments of Neurology, Biochemistry, Environmental Health, Behavioral Neuroscience Program; in addition, I have been an invited lecturer at the Harvard School of Public Health and the Massachusetts Neuropsychological Society. I have lectured to these classes in the following topics: Neurological Disorders and Neurotoxicology, Forensic Neuropsychology, Introductory Toxicology, Forensic Toxicology, and Neurotoxicity.

C. Overview of General Causal Inference in Science

1. This report presents my expert opinions on the role of Dan Allen's exposure to neurotoxic chemicals in May/June 2001 to the onset of, and death from ALS. So in effect, I examine two "big picture" questions: (a) whether the neurotoxic chemicals to which Mr. Allen was exposed are capable of altering or hastening the course of a neurodegenerative disease like ALS (we can refer to this as "General Causation"); and (b) whether this exposure was at least a substantial contributing cause to hastening the course of Mr. Allen's ALS (we can refer to this as "Specific Causation"). Before discussing my opinions, it may be valuable to briefly discuss the principles of General causal inference in science.

2. General Causation in science is an inference, a judgment based upon observational and experimental deductions as well as an understanding of the general laws of nature.

3. It is simply common sense that a single study is generally not sufficient for a causal inference. That is why the conclusions of most studies, no matter how large or small, speak in terms of their results "suggesting" that, for example, A is implicated in B. Published and peer-reviewed scientific studies almost never speak in language of "causation". So, as will be seen in this report, many studies are cited which make "suggestions" based upon well-designed and carried out methods. These studies, along with other methods of the scientific process, then form the basis for making a causal inference. Another way of thinking of the use of the word "suggests" when it appears in scientific literature is, "provides evidence in support of".

4. So, as a scientist, I am obligated to consider all available scientific evidence in assessing a causal inference. That includes large epidemiologic case-control studies, but also the smallest experimental studies looking at a handful of rats (or even just-looking at molecules), or anecdotal reports of events occurring in a few persons, as well as the pharmacology, toxicology, biologically plausible theories and mechanisms of actions. The fact that a study has flaws or is not "statistically significant" does not mean the study should be disregarded; indeed, it is scientifically inappropriate to fail to consider the cumulative effect of all scientific evidence.

5. In the real world, scientists and physicians infer causation from the totality of several lines of evidence that, together, comprise the body of existing scientific data. That is precisely what I have done here.

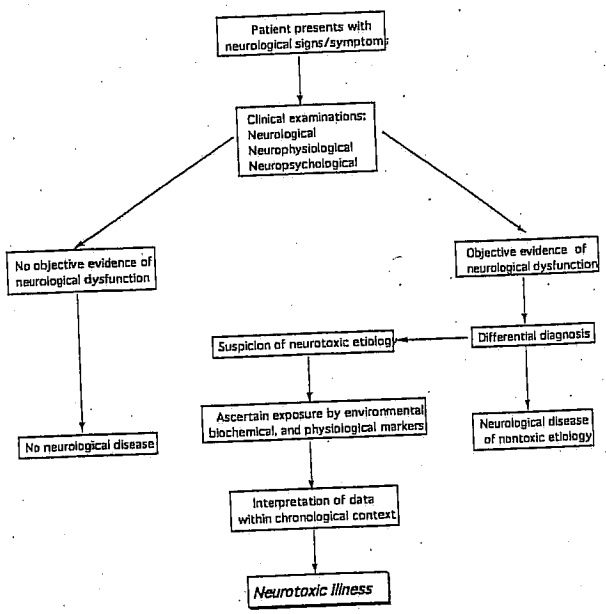
D. The Generally Accepted Scientific Method for Assessing Causation in Neurotoxicity Legal Cases

1. Just as there is an accepted method in assessing General Causation, so too there is a generally accepted method in neurotoxicity cases to assess Specific Causation.

2. It so happens that Dr. Feldman and I developed the diagnostic algorithm for this assessment. In our textbook, Occupational and Environmental Neurotoxicology (Lippincott-Raven 1999), we proposed a method for assessing specific causation in cases like that of Dan Allen. Our method has been received by scientific community and has been published in peer-reviewed journals without criticism. For example, we presented our model in the well-respected and peer-reviewed professional series, Neurologic Clinics in May 1999, in an article entitled, "Approach to Neurotoxicity Tort Cases". This article was invited by the editor of this series in recognition of our expertise in the area.

3. As it has now withstood the test of time for more than seven years, it can be considered generally accepted.

4. This can be diagrammed as follows:



5. I have followed this generally accepted method for assessing Specific Causation in the case of Dan Allen, as discussed below.

E. My Factual Assumptions

I have been asked to assume the following facts as relate to my consideration of this case:

1. In May/June 2001, Dan Allen was the head coach of the football program at the College of the Holy Cross. He was 45 years old and in good physical health. There was no history of ALS in his family.

2. In late May through early June, 2001, employees of Martin Surfacing re-surfaced the gym floor in the building known as the Field House at the college. Mr. Allen's office was located on the second floor of the Field House.

3. Mr. Allen was present throughout the course of the re-surfacing work.

4. The workers performing the re-surfacing made use of several chemicals, all as listed on certain MSDS sheets provided to me. These chemicals included toluene, xylene, methyl isobutyl ketone, ethyl benzene, titanium dioxide, propyleneglycol methylether acetate, dipropyleneglycol methylether acetate, isophorone diisocyante, methylenebis cyclohexylisocyanate, and Stoddard solvent (Stoddard solvent is a petroleum distillate fraction containing C_7—C_{12} hydrocarbons, primarily straight-chain and branched-chain alkanes and cycloalkanes; it may also contain up to 20% aromatic hydrocarbons.).

5. During the re-surfacing work, Mr. Allen complained of and exhibited signs of neurological dysfunction, including headaches, dizziness and nausea. Other personnel from the college who worked and were present in the Field House during the re-surfacing work experienced similar problems.[1] It is important to note that the symptom of nausea is common response of the brain to excessive blood levels of a toxic chemical. This response occurs to facilitate expulsion of the offending toxic agent. Volunteers exposed to toluene developed slight nausea and lassitude at a concentration of 600 ppm (this is 3 times the OSHA PEL of 200 ppm and 100 ppm greater than the maximum peak concentration permissible by OSHA) [Clayton and Clayton in Patty's Industrial Hygiene and Toxicology, 1981-1982, p. 3283; Hathaway, Proctor, Hughes, and Fischman, Proctor and Hughes' chemical hazards of the workplace. 1991, p. 546].(http://www.osha.gov/SLTC/healthguidelines/toluene/recognition.html) (also see 29 CFR 1910.1000)

F. My Clinical Examination of Dan Allen

In addition to the above assumptions, along with Dr. Joseph Jabre, I had the important opportunity to meet Dan Allen, and conduct a clinical neurological examination of his condition prior to Mr. Allen's death. A summary of that examination follows:

1. Mr. Daniel Allen sought consultation with the Environmental and Occupational Neurology Program at the Boston University School of Medicine for possible toxic exposure related neurological symptoms on April 13, 2004. Mr. Allen is a 48 year-old left-handed gentleman with no significant past medical history. Prior to his early retirement due to his physical limitations related to his neurological manifestations, Coach Allen (as he is known by his peers) was the head football coach at Holy Cross.

[1] I have relied on the affidavits of one of the floor refinishers, and several co-workers of Coach Allen, as well as Mr. Allen's written journals and the deposition of Mrs. Allen. The affidavits are contained here; the other items I understand are in the possession of defense counsel.

2. Coach Allen's history revealed unwitting occupational exposure that occurred in May-June of 2001 when the gym floor at the college where he was employed was refinished. The refinishing process took at least one full workweek to complete. During the refurbishment process, Coach Allen worked in his office located adjacent to the gym, and experienced acute symptoms of dizziness, headaches, and disorientation. Other people in the area reportedly had similar acute symptoms. One month later, while he was on vacation, he experienced diarrhea, which improved spontaneously. Upon returning to work from his vacation he again experienced symptoms of headaches and dizziness similar to when he was first exposed although no refurbishment work was actively being performed on the gym floor at this time. Around this same time Coach Allen began to experience symptoms of fatigue and weakness for which he sought medical consultation with his primary care physician and a neurologist. He was started on Paxil at this time. He was seen by Dr. David Chad at the University of Massachusetts, Worcester and Dr. Russell at the Lahey clinic who did an EMG on him in February 2002. He also had CSF studies and a head MRI. In September 2001, he developed fasciculations in the lower extremities, which spread to the arms and now have decreased. He became wheelchair bound in the spring of 2003. He is currently wheelchair bound with contracture of hands and feet. He also has hypothyroidism.

3. On clinical neurological exam, Coach Allen spoke softly and ran out of breath easily but was nevertheless able to provide a good history with assistance from his wife and his friend, Kate. Cranial nerves II-XII were all normal except for tongue atrophy and fasics. DTRs were 2+ KJ, 0 AJ, 1-2+ BJ, 1+ BRJ. Toes? + Hoffman's. Strength exam revealed generalized weakness in both the upper and lower extremities. Hands and feet were curled and difficult to examine. Sensory exam shows, mild decrease to pinprick in lower extremities. Cerebellar exam could not be performed due to patient's motor limitations.

G. Clinical Overview of ALS

A general discussion about ALS will be helpful in understanding the opinions presented in this report.

1. The National Institute of Neurological Disorders and Stroke (NINDS) defines ALS as follows: Amyotrophic lateral sclerosis (ALS), sometimes called Lou Gehrig's disease, is a rapidly progressive, invariably fatal neurological disease that attacks the nerve cells *(neurons)* responsible for controlling voluntary muscles.

2. In ALS, both the upper motor neurons and the lower motor neurons degenerate or die, ceasing to send messages to muscles. Unable to function, the muscles gradually weaken, waste away, and twitch. Eventually the ability of the brain to start and control voluntary movement is lost.

3. Individuals with ALS lose their strength and the ability to move their arms, legs, and body. When muscles in the diaphragm and chest wall fail, individuals lose the ability to breathe without ventilatory support.

4. The disease does not affect a person's ability to see, smell, taste, hear, or recognize touch, and it does not usually impair a person's thinking or other cognitive abilities. However, several recent studies suggest that a small percentage of patients may experience problems with memory or decision-making, and there is growing evidence that some may even develop a form of dementia.

5. Approximately 20% of familial ALS cases are associated with mutations in SOD1, the gene encoding Cu/Zn-superoxide dismutase (CuZnSOD) (Rosen et al., 1993). The cause of sporadic ALS on the other hand is not known, and scientists do not yet know why sporadic ALS strikes some people and not others.

6. This last point is important for this expert report. I do NOT offer the opinion in this case that Dan Allen's chemical exposure caused his ALS. It is my opinion, to a reasonable degree of certainty, that Mr. Allen was genetically predisposed to develop ALS and would likely have seen the course of ALS progress fatally, later in life. It is my opinion to a reasonable degree of certainty that Mr. Allen's chemical exposure hastened an early onset of his ALS.

H. Review of Epidemiology Addressing Chemical Exposure and ALS

1. Epidemiology is generally and simply defined as the study of the patterns, causes and control of diseases in sample populations.

2. When relevant epidemiology is available, it can be a useful tool and must be considered in a scientist's General Causation assessment. Epidemiology is not useful to assess so-called Specific Causation.

3. Many epidemiological studies have focused on elucidating the etiology of ALS, and therefore have asked whether chemicals "cause" or "trigger" the disease. Although numerous solvents and other industrial chemicals have neurotoxic properties, past exposure to these agents is often difficult to quantify and validate making these studies difficult to design and interpret.

4. Nevertheless, Siddique and colleagues (see Saeed et al. 2006) recently concluded based on the findings of their most recent study that there is evidence of a significant association of variants in the paraoxonase gene with sporadic ALS and that this is compatible with the hypothesis that *environmental toxicity in a susceptible host may precipitate ALS*.

5. Several case-control studies have evaluated the risk of ALS among those reporting past occupational exposure to solvents. According to a report prepared

by Noonan et al., 2002 for the *Agency for Toxic Substances and Disease Registry* (ATSDR) the epidemiologic literature offers some support for an association between the risk for ALS and past exposure to organic solvents.

6. Unfortunately, most of these studies suffer from deficiencies with regard to exposure characterization and chemical specificity. A study in the United States reported a small but statistically significant elevated risk of ALS among those who self-reported solvent exposure. Although the investigators found no elevated risk when overall solvent exposure was assessed by an expert panel review of occupational histories, the expert panel assessment of occupational exposure to more specific groups of chemicals found elevated risk estimates for alcohols or ketones; benzene, ***toluene***, or ***xylene***; and cleaning solvents or degreasers (McGuire et al., 1997).

7. McGuire (1997) is the only study that evaluated the risk of ALS from exposure to individual, specifically identified, volatile organic compounds and it is interesting to note the two of the solvents to which Mr. Allen was exposed are among those associated with an increased risk.

8. While it is not the position of this document that any chemical causes ALS, the role of chemical exposures as modifying factors in the clinical course of the disease is demonstrable.

9. Although polymorphisms in enzymes involved in the metabolism of chemicals and age at onset of ALS has been studied, there are very few published reports that have looked specifically at the relationship between age at onset of ALS and antecedent events such as exposure history (Orru et al., 1999; Provinciali L, Giovagnoli, 1990; Saeed et al., 2006).

10. Among the possible reasons for the paucity of data is the simple fact that the answer is fairly intuitive as will be discussed further below (i.e., if exposure to neurotoxicants kills neurons and ALS kills neurons then the additive effects of the two events occurring in the same individual should be a younger age at onset of the disease).

11. The second reason is funding limitations; why spend money and time looking at factors that modify the clinical course of the disease when the more important question of what causes ALS has not yet been answered?

12. Moreover, and importantly, the only entities with the financial means to conduct epidemiological studies to examine the role of a specific chemical in altering the course of ALS, is the chemical industry, and while industry has the means to conduct such a study, it does not have the motivation to do so, for obvious business reasons. The reverse is true for the pharmaceutical industry, which invested millions of dollars on human clinical trials (the industry equivalent of

epidemiological studies) looking for chemicals that can slow the course of the disease, again for obvious business reasons.

13. Finally, a study that would examine the role of a specific chemical and its association with a disease like ALS, would be very expensive (on the order of millions of dollars) and take many years to complete.

14. Nevertheless, there has been a recent shift among those involved in neurodegenerative disease research in general toward elucidating the relationships between exposure history, genetics, and age at disease onset as the failure to identify a common genetic cause makes it increasing plausible that these types of disease involves multiple factors (Racette et al., 2001; Pezzoli et al., 2000; Wilk et al., 2006).

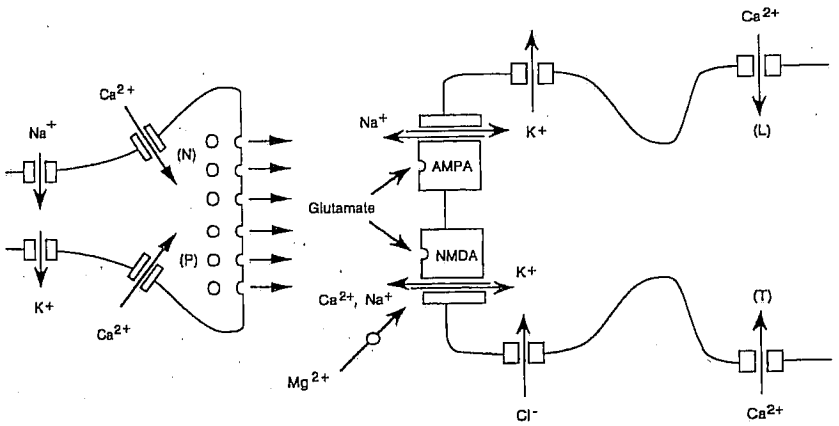
15. So, while there are no epidemiologic studies which contradict the position taken in this paper, there is admittedly little epidemiologic data which is directly on point. This is often the case when examining the neurotoxicity of chemicals, and yet scientists are constantly able to arrive at sound and rational causal inferences, through the scientific method, as I have done here.

I. Pathogenesis of ALS: Review of Generally Accepted Mechanisms of Action

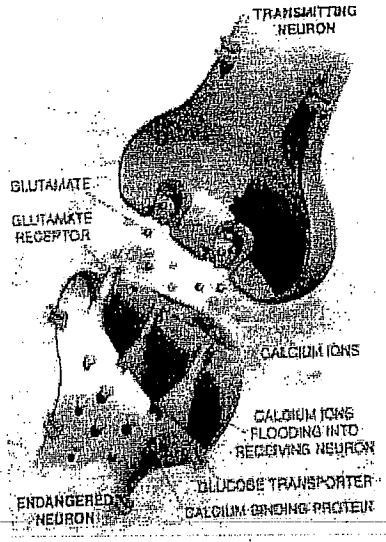
The following presents the generally accepted mechanisms by which neurodegeneration occurs in ALS (glutamatergic neurotransmission and oxidative stress).

I begin with some important concepts necessary to understand the neuroscience at issue, and then discuss the specific mechanisms at issue.

1. Communication between nerve cells is referred to as *neurotransmission*, which is mediated by *chemical messengers* known as neurotransmitters. Glutamate is an example of an excitatory neurotransmitter (i.e., a neurotransmitter that excites the next neuron in the chain of command). Upper motor neurons communicate with lower motor neurons by releasing glutamate. During glutamatergic neurotransmission (i.e., neurotransmission mediated by glutamate), glutamate released from the presynaptic or upstream neuron binds to and activates receptors located on the surface of the postsynaptic or downstream neuron. Activation of these excitatory glutamate receptors results in an influx of sodium (Na^+) and calcium (Ca^{2+}) ions into the cell body, which in turn causes the neuron to release its neurotransmitters (see Figure below). And so, the process continues until the final cell in the chain of command is activated (e.g. a muscle cell is signaled to contract).



2. *Excitotoxicity* is a type of neuronal degeneration mediated by over-stimulation of glutamate receptors. Experimental evidence indicates that glutamate mediated excitotoxicity contributes to neuronal damage in a number of neurodegenerative disorders including amyotrophic lateral sclerosis (ALS). The role of glutamate mediated excitotoxicity in ALS is related to the fact that upper motor neurons are glutamatergic (i.e., communicate with lower motor neurons by releasing glutamate). *Elevated extracellular glutamate* concentrations can occur when the release from presynaptic terminals is augmented or when re-uptake is insufficient. Adequate re-uptake is normally assured by glutamate transporters present in neurons and astrocytes. Elevated glutamate concentrations can also occur when glutamate is released from injured glutamatergic neurons. The release of glutamate into the extracellular space results in excitotoxic death of surrounding neurons (see figure below). This type of collateral damage is involved in the spread of the neurodegeneration following stroke and is associated with neurodegeneration in ALS (Van Den Bosch et al., 2007). As neurons die, the glutamate released is able to induce this excitotoxic cascade in more than one adjacent neuron. As more and more neurons die and more and more glutamate is released, the process begins to snowball and the progression of the disease increases. At a critical point, when the majority of the neurons have died, the disease essentially ceases to progress further.



3. Assuming that Mr. Allen's chemical exposure resulted in the death of even a single motor neuron, then the exposure contributed to the progression of his disease (It is my opinion that the exposure was at least a substantial contributing factor as expressed in this report). More importantly, the death of each glutamatergic motor neuron would result in the release of glutamate, which spills into the extracellular space where it reacts with receptors on adjacent neurons and can thereby induce something called "apoptosis" via excitotoxicity, thereby aggravating an already relentlessly progressive neurodegenerative process mediated by the increased glutamate released in association with the death of neurons due to ALS. This can effectively be thought of as being like a snowball rolling down a hill in that each dying neuron contributes to the death of other neurons. The only FDA approved pharmaceutical agent for treating ALS, riluzole, is administered in an attempt to slow this process.

4. *Apoptosis* is a form of programmed cell death in which the cell self-destructs when stimulated by the appropriate trigger. It is a genetically programmed event that can be triggered by a variety of internal or external stimuli. Apoptosis is characterized morphologically by cell shrinkage, membrane blebbing, chromatin condensation and fragmentation. These changes distinguish apoptosis from cell death by *necrosis*, which refers to the morphological changes associated with abrupt cell death as occurs following ischemia or physical trauma. In contrast to apoptosis, necrosis, is associated with disruption of cellular respiration and osmotic pressure, and with swelling that ultimately causes the cell to rupture.

5. *AMPA receptors are a type of glutamate receptor. AMPA mediated excitotoxicity is aggravated by chloride influx.* It has been shown in cultured rat spinal motor neurons that chloride influx aggravates Ca^{2+}-dependent AMPA receptor mediated motor neuron death. The membrane depolarization caused by AMPA receptor stimulation results in Cl^- influx through 5-nitro-2(3-phenylpropyl-amino) benzoic acid- and niflumic acid-sensitive Cl^- channels. This Cl^- influx aggravates excitotoxic motor neuron death by two mechanisms: (1) It increases the AMPA

receptor conductance; and (2) it also results in an elevation of the Ca^{2+} driving force through a partial repolarization. As a consequence, Cl^- ions can play a vital role in glutamate-mediated excitotoxicity (van Damme et al., 2003).

6. *Although Cl^- influx normally suppresses neuronal excitability and thereby counteracts the action of excitatory neurotransmitters such as glutamate, Cl^- influx during exposure to pathological amounts of glutamate can amplify the excitotoxic action of glutamate on motor neurons. Co-administration of GABA enhances the Cl^- influx during AMPA receptor stimulation and this results in an increased Ca^{2+} influx and enhanced cell death. These observations suggest that concomitant GABAergic stimulation may aggravate excitotoxic motor neuron death. This effect of Cl^- influx on excitotoxicity does not seem to be unique to motor neurons, as similar results were found in cerebellar granule cells.* (van Damme et al., 2003). I address Toluene in detail below, but it worth noting here that, like ethanol, Toluene reversibly enhances $GABA_A$ receptor-mediated synaptic currents in rat hippocampal slices (Beckstead et al., 2000). When GABA binds to the $GABA_A$ receptor the channel is opened and chloride ions enter the neuron (i.e., chloride influx is enhanced).

7. These findings provide evidence for just one of the mechanisms by which exposure to toluene can contribute to excitotoxic upper motor neuron death.

8. Unfortunately, it is much more likely that the chemical exposure Mr. Allen experienced resulted in the death of more than one motor neuron and that this process involved more than one mechanism of neurotoxicity. This neuronal loss would have been induced by direct neurotoxic effects as cited above and indirectly by the chemical exposure interfering with the ability of his body to scavenge "free radicals" and attenuate "oxidative stress" which importantly has been implicated in the progression of ALS (Chi et al., 2007; McDermott et al., 2007).

9. By definition a *free radical* is any atom (e.g. oxygen, nitrogen) with at least one unpaired electron in the outermost shell. Free radicals are highly reactive due to the presence of unpaired electron(s).

10. *Oxidative stress* is a commonly heard term that refers to the adverse effects that *reactive oxygen species (ROS) such as hydrogen peroxide and the free radicals super oxide and the hydroxyl radical have on the body.* Antioxidants such as vitamin E and vitamin C scavenge reactive oxygen species and prevent them from damaging tissues. Reactive oxygen species are chemicals that possess a lone electron. Electrons like to be paired with other electrons. When this does not happen quickly enough they will steal an electron from any nearby source. One such source is the lipid rich cell membranes of neurons. This reaction results in damage to the cell membrane referred to as lipid peroxidation, which is one type of neuronal cell damage that results from oxidative stress and is characterized by addition of a peroxide group to the cell membrane, which in turn alters the

membrane structure and its ability to function properly. Reactive oxygen species also damage mitochondrial membranes and thereby disrupt cellular respiration, which is critical to cell viability. ROS can also damage DNA and disrupt protein synthesis (Halliwell, 2006).

11. Approximately 20% of familial ALS cases are associated with mutations in SOD1, the gene encoding Cu/Zn-superoxide dismutase (CuZnSOD) (Rosen et al., 1993). Studies suggest that SOD1 mutation leads to cell death not only through a reduction in clearance of superoxide radical but through some other as yet undefined mechanism. Recently, mitochondrial-produced oxygen radicals have been found to play a critical role in mutant SOD1-mediated neuronal toxicity suggesting that mitochondrial-produced free radicals may be potential therapeutic targets in ALS (Zimmerman et al., 2007).

12. Studies suggest that free radicals both decrease depolarization-induced vesicular release and enhance basal, nonvesicular release of glutamate. In order to evaluate the contribution of oxidative reactions to this effect, the actions of the oxidizing agent chloramine-T on synaptosomal release of excitatory amino acids have been assessed. Basal and depolarization evoked [3H]D-aspartate release were found to be calcium-independent and nonvesicular. Chloramine-T pretreatment significantly increased basal release, while having no effect on high K(+)-evoked release. These data suggest that an oxidative process can mimic the free radical increase of basal release, as well as the decrease in synaptic potentials. On the other hand, calcium-independent-evoked release may involve a different mechanism. These results demonstrate that under basal, nondepolarizing conditions, oxidative stress exerts an adverse effect on the presynaptic nerve terminal, resulting in an increased release of potentially damaging excitatory amino acid neurotransmitters such as glutamate (Gilman et al., 1993).

13. Studies in mice expressing the mutant form of SOD1 indicate that supplementation with vitamin E can slow disease onset suggesting that an increase in oxidative stress is associated with disease onset and that this process can be attenuated by antioxidants (Gurney et al., 1996).

14. I will spend a moment also discussing something called "p75 neurotrophin receptor (p75NTR)". p75NTR is a member of the tumor necrosis factor receptor superfamily and acts as a death receptor, inducing apoptosis in several neuronal populations (Kust et al., 2003; Pehar et al., 2006). p75NTR facilitates apoptosis during development and after injury to the CNS. Recent studies suggest that modulation of p75NTR by small molecule ligands targeting this receptor might constitute a novel strategy for preventing motor neuron degeneration (Pehar et al., 2006). Acute toluene administration in rats induces a significant increase in the numbers of neurons immunostained for p75NTR in several brainstem regions, such as the raphe magnus and the nucleus of the solitary tract, as well as in the lateral reticular, gigantocellular, vestibular and ventral cochlear nuclei, without any in the facial and spinal trigeminal nuclei and the dorsal horn of the spinal

cord. *These data suggest that p75NTR could be involved in toluene-induced neurotoxic effects as well as ALS (Pascual et al., 2004; Kust et al., 2003; Pehar et al., 2006).*

15. To counteract ROS- and electrophile-mediated injury, cells can induce a number of genes encoding phase II detoxifying enzymes and antioxidant proteins. The transcription factor nuclear factor-erythroid 2-related factor 2 (Nrf2) regulates the genetic expression of phase II detoxification enzymes such as glutathione-S-transferase and antioxidant proteins through an enhancer sequence referred to as the antioxidant-responsive element (ARE). Studies have shown that an increase in glutathione biosynthesis induced by Nrf2 activation in astrocytes prevents p75NTR-dependent motor neuron apoptosis (Vargas et al., 2006) suggesting that modulating glutathione levels may alter the progression of ALS. It is important to note that glutathione levels are reduced in liver and brain regions from toluene-treated rats (Mattia et al., 1993).

16. As I have already discussed, ALS is associated with a loss of motor neurons. Exposures to neurotoxic chemicals can also kill motor neurons. It is therefore reasonable to expect that these two factors, which can independently kill neurons, might interact in some way. Simply put, if you need to kill 80% of the motor neurons you are born with in order to experience overt symptoms of ALS then any factor which can increase or decrease the natural progression of neuronal loss up to this critical point would be expected to decrease or increase the age at onset of ALS. With this in mind, pharmaceutical companies are working diligently to discover drugs that can prevent neuronal loss and thereby slow the progression of ALS. This work is contingent upon using *in vitro* screening studies (e.g. high-throughput electrophysiology) to identify possible candidate compounds based on the putative mechanisms involved in ALS as defined in the basic scientific literature. These "hits" are then tested and optimized in animal models of ALS before being approved for human clinical trials. Thus far, researchers have identified at least one compound rulizole, which is believed at this time to provide neuroprotection via inhibition of glutamate-mediated excitoxicity which can slow the progression of ALS.

17. A logical question when confronted with this knowledge is, "if a compound like rulizole can slow the progression of ALS can other compounds make it progress more rapidly"? Not surprisingly, the same *in vitro* studies used to identify "hits" in drug discovery studies and the same animal models used to optimize these hits before they are approved by the FDA for human use in Phase I clinical trials indicate that neurotoxicants such as toluene act in ways that would absolutely make them hasten the course of ALS. For example treatment of neurons with toluene (1 mM; 4 days) increased whole-cell responses to exogenously applied NMDA, reduced those evoked by GABA but did not alter responses generated by kainic acid. Immunoblot analysis revealed that toluene exposure increased levels of NR2A and NR2B NMDA receptor subunits with no change in NR1. Immunohistochemical analysis with confocal imaging showed that toluene-treated

neurons had significant increases in the density of NR1 subunits as compared with control neurons. Toluene exposure increased the amplitude of synaptic NMDA currents and decreased those activated by GABA. The results from this study suggest that exposure to toluene induces compensatory responses in the functional expression of ion channels that regulate neuronal excitability (Bale et al., 2005).

18. The pathogenesis of neurodegenerative diseases such as ALS most likely involves a genetic predispositions acting in concert with environmental insults. To test this hypothesis Andreassen and colleagues (2001) examined whether transgenic mice with the G93A mutation in Cu,Zn superoxide dismutase show increased vulnerability to either 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) or 3-nitropropionic acid (3-NP). Compared to littermate controls G93A transgenic mice showed a greater loss of striatal dopamine, DOPAC, and HVA at 50, 70, and 120 days of age following administration of MPTP; however, cell loss in the substantia nigra was not greater. The G93A transgenic mice showed significantly increased vulnerability to striatal lesions produced by 3-NP compared with littermate controls at 120 days of age. The finding that G93A mice show increased vulnerability to mitochondrial toxins further implicates mitochondrial dysfunction in the pathogenesis of neuronal death in these mice. *The findings support the hypothesis that a genetic defect can increase susceptibility to environmental toxins and that this may play a role in the pathogenesis of neurodegenerative diseases* (Andreassen et al., 2001).

19. In summary, I have presented the recognized and accepted mechanisms by which ALS is posited to cause the death of motor neurons. The well-recognized and important roles of oxidative stress and glutamatergic excitotoxicity are described in detail. I have defined the necessary terms for the reader so he or she can appreciate the materials presented herein. I have related this material to the current therapies for ALS for the purpose of demonstrating how chemicals can be used to positively alter the course of the disease.

J. Review of the Generally Accepted Mechanisms by which Toluene Causes Neurotoxicity

So, having examined the mechanisms by which neurodegeneration occurs in ALS, I now review the generally accepted means by which neurotoxic chemicals such as Toluene also cause neurodegeneration. First, I review Mr. Allen's chemical exposure.

1. Mr. Daniel Allen experienced an unwitting occupational exposure to neurotoxic chemicals in June of 2001 when the gym floor was being refinished at the college where he was employed. The refinishing process took one to two workweeks to complete. During the refurbishment process, Mr. Allen worked in his office, which was located just above the gym. He reportedly experienced acute symptoms of dizziness, headaches, and disorientation. Other people working in the area reported similar symptoms.

2. The Material Safety Data Sheets (MSDS) sheets provided by Martin flooring indicate that some of the products used in this process contained neurotoxic solvents. For example, the solvents contained in the Moisture Cure Coatings may cause damage to the nervous system with repeated or chronic exposures. Among the chemicals reportedly used during the refinishing of the gymnasium floor were the solvents methyl isobutyl ketone, xylene, toluene and Stoddard solvent (white spirit/mineral spirit). Although these solvents differ with respect to their individual neurotoxic potentials, exposure to mixtures of these chemicals increases the risk for neurotoxic effects. This is due in part to competitive inhibition of enzymes involved in detoxification process. Some of the compounds also share toxic mechanisms of action so their effects can be additive. More importantly the combined effects of exposures to compounds with different mechanisms of action can be even greater than the sum of their individual effects (synergism). The net result is that exposures to mixtures of neurotoxic compounds can result in adverse effects even when exposures limits for individual compounds have not been exceeded (Noraberg and Arlien-Soberg, 2000; Dobrev et al., 2002).

I will look at each of these chemicals (Stoddard Solvent, Xylene and Toluene) with an emphasis on the latter:

Stoddard Solvent

3. Stoddard solvent (white spirit/mineral spirit) is the most widely used solvent in the paint industry. Exposure to Stoddard solvent can cause dizziness and headaches. An increase in *oxidative stress has been associated with exposure to Stoddard solvent* (Lam et al., 1994).

Xylene

4. *Exposure to xylene has been associated with increased oxidative stress and a decrease in glutathione levels* (Pathirante et al., 1986; Piotrowska et al., 2002). Toluene and xylene are chemicals present in various laboratory and other industrial products. Their toxicity to the nervous system is well documented. The in vitro effects of toluene and xylene on the respiration of succinate-energized isolated rat liver mitochondria, membrane potential, Ca(2+) release, reactive oxygen species (ROS), and ATP levels as well as Ca(2+)-dependent, cyclosporine A-sensitive mitochondrial swelling, an indicator of mitochondrial permeability transition (MPT) have been studied. At 0.5-2.5 and 0.25-1mM concentrations respectively, toluene and xylene stimulated state 4 respiration in apparent association with mitochondrial membrane potential dissipation and Ca(2+) release; these actions of both solvents are consistent with mitochondrial uncoupling. At higher concentrations (2.5 and 5mM, respectively) toluene and xylene also inhibited state 3 respiration. At 0.1-1mM concentrations, xylene elicited significant increase of ROS generation and partly Ca(2+)-dependent cyclosporine A-sensitive mitochondrial swelling. At 1 mM concentration, toluene

or xylene caused depletions of mitochondrial ATP, amounting to 66.3% and 40.3%, respectively; depletions were only slightly dependent on Ca(2+). It was concluded that mitochondrial uncoupling via ATP depletion might be responsible for the cell toxicity of toluene described earlier and in particular, of xylene. In the case of xylene, mitochondrial ROS generation and MPT also appear to be involved (Revilla et al., 2007). Depletion of glutathione levels due to xylene exposure may also induce p75NTR-dependent motor neuron apoptosis (Vargas et al., 2006).

Toluene

5. Toluene is a volatile organic solvent that is used in a variety of commercial, industrial and household products, including but not limited to adhesives, varnishes, lacquers, paints, and paint thinners. Exposure to toluene occurs in occupational and non-occupational situations. In addition toluene is commonly abused representing a significant worldwide health and social burden (Feldman, 1999). The Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) for toluene is 200 ppm.. The OSHA Ceiling Concentration is 300 ppm (assessed as a 15-minute time weighted average exposure) and the maximum peak concentration above the acceptable ceiling concentration for an 8-hour shift is 500 ppm for a maximum duration of just 10 minutes (29 CFR 1910.1000).

6. A meta-analysis of the toluene data about shock avoidance behavior in rats and choice reaction time in humans suggests that a 10% change in rat avoidance behavior occurs at a blood concentration of toluene 25 times higher than the concentration at which a 10% change in human choice reaction time occurs. In contrast, in vitro studies of nicotinic acetylcholine receptors indicated that human and rat receptors do not differ in sensitivity to toluene. Analysis of other dose-response relationships for visual and cognitive functions in rats suggests that the apparent difference between rats and humans may be driven by the specific endpoints measured in the two species rather than by inherent differences in sensitivity to toluene (Bushnell et al., 2006).

7. Just like Mr. Allen, painters and other workers exposed to solvents such as toluene experience acute symptoms of dizziness, nausea, depression, and fatigue (Welch et al., 1991; Wang and Chen, 1993; Kishi et al., 1993). Brain magnetic resonance imaging shows cerebral and hippocampal atrophy as well as a loss in brain volume in toluene/solvent abusers as well as painters (Welch et al., 1991; Deleu and Hanssens, 2000; Kamran and Bakshi, 1998; Yamanouchi et al., 1995, Feldman et al., 1999).

8. "There seems to be a statistically significant association between work in the leather industry and subsequent development of motor neuron disease. The reason for this association may be occupational exposure to solvents, which may damage

motor neurons either directly or through activation of latent virus" (Hawkes et al., 1989).

9. Toluene is a known neurotoxicant used in lacquers, glues and paints. Exposure to toluene causes both reversible and irreversible changes in the central nervous system. The effects of toluene inhalation on some specific enzymes and glutamate and γ-aminobutyric (GABA) receptor expression and binding in defined parts of the rat brain have been studied following several exposure schemes (Williams et al., 2005).

10. As discussed above, the p75 neurotrophin receptor (p75NTR) is a member of the tumor necrosis factor receptor superfamily and acts as a death receptor, inducing apoptosis in several neuronal populations. Reduced p75NTR expression delays disease onset in female SOD1 transgenic mice (Kust et al., 2003). Improved survival in female mice was not correlated with increased motoneuronal survival, but with less astrocytic activation in lumbar ventral spinal cord, as shown by glial fibrillary acidic protein immunohistochemistry. Other studies have also shown that an increase in glutathione biosynthesis induced by Nrf2 activation in astrocytes prevents p75NTR-dependent motor neuron apoptosis (Vargas et al., 2006). Importantly exposure to toluene induces a significant increase in the numbers of neurons immunostained for p75NTR in several brainstem regions of rats and depletes glutathione levels (Pascual et al., 2004). *These data demostrate that p75NTR is implicated in toluene-induced neurotoxic effects as well as in the progression of ALS (Pascual et al., 2004; Kust et al., 2003; Pehar et al., 2006).*

Glutathione Levels Implicated in ALS and Toluene Neurotoxicity

11. Glutathione (GSH) is an extremely important cellular protectant. It directly quenches reactive hydroxyl free radicals, other oxygen-centered free radicals, and radical centers on DNA and other biomolecules. Glutathione is synthesized in the body from 3 amino acids: Cysteine, glutamine and glycine. Cysteine is one of the sulfur containing amino acids used for the synthesis of glutathione. N-Acetyl Cysteine (NAC) is the rate limiting amino acid for the production of glutathione within the cells of the body and it too is a powerful antioxidant and detoxifier. The thiol group is the active part of the molecule and serves as a reducing agent to prevent oxidation of tissues. Glutathione acts as one of the major detoxifiers in the body, but it must be in the *reduced form* to work properly. The unreduced form isn't metabolically active. Riboflavin, niacinamide, selenium, lipoic acid and glutathione reductase are all essential cofactors for generating *reduced glutathione*. When reduced GSH loses electrons the molecule becomes oxidized, and two such oxidized GSH molecules can linked together (dimerized) by a disulfide bridge to form glutathione disulfide or oxidized glutathione (GSSG). This linkage is reversible upon re-reduction. GSH is under tight homeostatic control both intracellularly and extracellularly. A dynamic balance is maintained between GSH synthesis, its recycling from GSSG/oxidized glutathione, and its utilization. GSH synthesis involves two closely linked enzymatically controlled

reactions that utilize ATP. First cysteine and glutamate are combined, by gamma-glutamyl cysteinyl synthetase. Second, GSH synthetase combines gamma-glutamylcysteine with glycine to generate GSH. As GSH levels rise, they self-limit further GSH synthesis; otherwise, cysteine availability is usually rate-limiting. GSH recycling is catalyzed by glutathione disulfide reductase, which uses reducing equivalents from NADPH to reconvert GSSG to 2GSH. *Direct attack by free radicals and other oxidative agents can deplete GSH.* The homeostatic glutathione redox cycle attempts to keep GSH repleted as it is being consumed. Amounts available from foods are limited (less than 150 mg/day) and thus oxidative depletion can easily outpace synthesis.

12. A motor neuron-like cell culture system and a transgenic mouse model have been used to study the effect of cellular GSH levels on motor neuron cell death. Exposure of NSC34 motor neuron-like cells to ethacrynic acid (EA) or l-buthionine sulfoximine (BSO) dramatically reduced the cellular GSH levels, and was accompanied by increased production of reactive oxygen species (ROS) measured by the dichlorofluorescin (DCF) fluorescent oxidation assay. In addition, depletion of GSH enhanced oxidative stress markers, AP-1 transcriptional activation, c-Jun, c-Fos and heme oxygenase-1 (HO-1) expression in NSC34 cells analyzed by a luciferase reporter, Western blotting and quantitative PCR assays respectively. Furthermore, depletion of GSH decreased mitochondrial function, facilitated apoptosis inducing factor (AIF) translocation, cytochrome c release, and caspase 3 activation, and consequently led to motor neuron-like cell apoptosis. In an ALS-like transgenic mouse model overexpressing mutant G93A-Cu, Zn-superoxide dismutase (SOD1) gene, it was shown that the reduction of GSH in the spinal cord and motor neuron cells is correlated with AIF translocation, caspase 3 activation, and motor neuron degeneration during ALS-like disease onset and progression. *Taken together, the in vitro and in vivo data presented in the current report demonstrated that decreased GSH promotes multiple apoptotic pathways contributing, at least partially, to motor neuron degeneration in ALS* (Chi et al., 2007).

13. Animal studies have demonstrated that toluene reduces GSH levels (Mattia et al., 1993). Workers exposed to benzene, toluene, xylene, hexane, ethylbenzene have significantly lower GSH concentrations ($p < 0.001$) compared to unexposed controls (Georgieva et al., 2002).

Oxidative Stress and Phase II Metabolic Enzymes Implicated in ALS and Toluene Neurotoxicity

Plasma malondialdehyde (MDA, a product of lipid peroxidation) levels and activity levels of the antioxidant enzymes gluthatione peroxidase (GSH-Px) and superoxide dismutase (SOD) in erythrocytes of people ($n = 18$) working with paint thinner containing toluene were ascertained as indicators of oxidative stress. Glutathione peroxidase is a compound involved in detoxification against peroxides and other xenobiotics. It is synthesized from selenium and cysteine.

14. The control group was composed of 18 healthy adults. There was a significant ($p < 0.001$) increase in plasma MDA levels and GSH-Px activity levels in people working with paint thinner compared with control subjects. Similarly, there was also an increase ($p < 0.05$) in the SOD levels of people working with paint thinner compared with controls. These observations suggest that paint thinner inhalation increases lipid peroxidation and consequently induces synthesis of antioxidant enzymes in an attempt to prevent damage to at risk cells (Halifeoglu et al., 2000).

15. Feldman and Ratner (1999) proposed that exposures to neurotoxicants interact with genetic predispositions that modify the ability of the body to metabolize and detoxify chemicals such that the clinical course of a neurodegenerative disease is hastened. Recently the interaction between neurodegenerative disease and genetics that my colleague and I predicted based on our expertise in this area at the time was confirmed by a Boston University study looking at the genes involved in the metabolism of toxic chemicals and age at onset of the neurodegenerative disease Parkinson's disease (Wilk et al. 2006). In this study Wilk and colleagues found an interaction between certain genes that encode for the enzyme glutathione-*S*-transferase and a younger age at onset of PD among persons exposed to herbicides. These findings and others contribute to the growing body of literature demonstrating that genetics factors can interact with exposures to chemicals to alter the clinical course of neurodegenerative diseases such as ALS and Parkinson's disease.

16. *Glutathione S-transferase* is an enzyme responsible for inactivation of a large variety of toxic electrophilic compounds and organic peroxides. GST activity and GST pi expression were also studied in patients with amyotrophic lateral sclerosis (ALS). Studies were conducted on cerebrospinal fluid (CSF), blood serum and peripheral blood mononuclear cells (PBMC) obtained from 40 ALS patients. CSF from 30 subjects without neurological diseases and blood from 40 healthy blood donors were used as controls. GST activity assayed with 1-chloro-2,4-dinitrobenzene (substrate for transferase activity) and cumene peroxide (substrate for peroxidase activity) was significantly decreased in PBMC of ALS patients, as well as the GST pi expression on both mRNA and protein level. The mean peroxidase activity was however significantly increased in CSF and serum of ALS patients with the specificity of 80% and 73%, and the sensitivity of 78% and 85%, respectively. *It can thus be concluded that the protective effect provided by GST is reduced in peripheral blood of ALS patients, and may increase their vulnerability to toxic effects of electrophilic compounds and organic peroxides.* Studies on a larger group are needed to answer the question whether GSH-Px determination may be implicated in the diagnosis of ALS (Kuzma et al., 2006).

17. The expression of the pi isozyme of glutathione-S-transferase (GST pi) was studied in spinal cord, motor and sensory brain cortex obtained from patients who died in the course of amyotrophic lateral sclerosis (ALS). The studies were performed on formalin-fixed, paraffin-embedded (FFPE) and freshly frozen tissues. The method of RNA isolation from FFPE was modified. A significant

decrease of GST pi-mRNA expression was found in cervical spinal cord and motor brain cortex of ALS subjects comparing to analogue control tissues ($P<0.01$), as well as in motor cortex of ALS subjects comparing to their sensory cortex ($P<0.05$). In spinal cords the decrease in GST pi-mRNA expression was accompanied by a decrease of GST pi protein level. *Results indicated lowered GST pi expression on both mRNA and protein levels in the regions of the nervous system affected by ALS. The non-properly inactivated by GST toxic electrophiles and organic peroxides may thus contribute to motor neurons damage* (Usarek et al., 2005).

18. Toluene and its metabolites have been studied with respect to their reactive oxygen species-enhancing potential in isolated systems and in vivo. The induction of reactive oxygen species (ROS) production was assayed in this study using the probe 2',7'-dichlorodihydrofluorescin diacetate (DCFH-DA). Intraperitoneal injection of toluene, benzyl alcohol or benzaldehyde caused a significant elevation in the rate of ROS formation within hepatic mitochondrial fractions (P2). In the brain, only toluene induced ROS formation, while benzyl alcohol and benzaldehyde did not have any effect. Glutathione (GSH) levels were depressed in liver and brain regions from toluene-treated rats. However, no such depression was evident in brains treated with toluene metabolites. P2 fractions from phenobarbital-pretreated rats exhibited a heightened ROS response when challenged with toluene, in vitro. Pretreatment of rats in vivo with 4-methylpyrazole, an alcohol dehydrogenase inhibitor, or sodium cyanamide, an aldehyde dehydrogenase inhibitor, prior to exposure to toluene, caused a significant decrease and increase, respectively, in toluene-stimulated rates of ROS generation in the CNS and liver. Electron spin resonance spectroscopy, employing the spin trap 5,5-dimethyl-1-pyrroline N-oxide (DMPO), was conducted. Incubation of the spin trap with P2 fractions and toluene or benzaldehyde elicited a spectrum corresponding to the hydroxyl radical. Incubation of benzaldehyde with aldehyde dehydrogenase produced a strong signal that was blocked completely by superoxide dismutase and inhibited partially by catalase, suggesting the presence of superoxide radicals and the involvement of the iron-catalyzed Haber-Weiss reaction leading to the production of hydroxyl radicals. Thus, ROS generation during toluene catabolism may occur at two steps: cytochrome P450 oxidation and aldehyde dehydrogenase oxidation. In addition, GSH may play an important role in protection against the induction of ROS generation in the CNS and liver following exposure to toluene (Mattia et al., 1993) as well as in p75NTR-dependent motor neuron apoptosis (Vargas et al., 2006) as previously cited.

19. The following study was designed to investigate the effects of chronic toluene inhalation in high concentration on lipid peroxidation, antioxidant enzyme activities and ultrastructural changes in the sciatic nerves of rats. Male Wistar albino rats (150-250 g) were divided in two experimental groups: the control and the toluene treated group ($n = 10$ for each). Toluene treatment was performed by inhalation of 3000 ppm toluene, in a 8 h/day and 6 day/week order for 16 weeks.

Blood and tissue samples were obtained for biochemical and histopathological investigation. The blood and sciatic nerves were assayed for toluene by gas chromatography. Toluene significantly increased blood and tissue malondialdehyde (MDA), and decreased tissue superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), but not tissue catalase (CAT) levels when compared with controls. Electron micrographs of sciatic nerve in the toluene group shows myelin destructions with onion-bulb and bubble form protrusion on the myelin sheath and axolemma border of myelinated axons. The area of injury on the myelin sheath were measured by Image-Pro Plus. Mean of the injury area were estimated 34% each myelin. These findings indicate that chronic toluene inhalation might be involved with free radical processes (Coskun et al., 2005).

20. The following study investigated glial reactivity in hippocampus, cortex and cerebellum and the expression of glial fibrillary acidic protein (GFAP) after exposure of rats to toluene vapor (3000 ppm) for 45 days. The protective effects of melatonin whish is neuroprotective against free radical damage was also examined. Western blots demonstrated a marked elevation in total Glial Fibrillary Acidic Protein (GFAP), a specific marker for astrocytes, induced by thinner fume inhalation in the hippocampus ($P<0.001$), cortex ($P<0.01$) and cerebellum ($P<0.05$) of rats. Melatonin administration prevented the increase of total GFAP induced by thinner fume inhalation. Thinner exposure caused a significant increase of lipid peroxidation products (malondialdehyde and 4-hydroxyalkenals) in all brain regions ($P<0.01$ for each region), and this elevation was also was inhibited by melatonin. Furthermore, melatonin augmented glutathione levels in all brain regions ($P<0.05$ for each region) investigated. In conclusion, melatonin treatment may provide neuroprotection against toluene neurotoxicity by increasing the survival of glial cells possibly by directly scavenging ROS and by indirectly augmenting their antioxidant capacity (Baydas et al., 2003).

21. Bjornaes and Naalsund, (1988) studied the activities of the transmitter synthesizing enzymes glutamic acid decarboxylase (GAD), choline acetyltransferase (ChAT) and aromatic amino-acid decarboxylase (AAD) as markers for permanent loss of neuronal activity. Catecholaminergic neurons showed a 50% reduction in the brainstem after 4 weeks of exposure to 250 and 1000 ppm toluene. Following 500 ppm of toluene, 16 h/day for 3 months, a general increase in the activities was seen. This is most probably due to a reduction in total protein content, to which the activities were related. The neurotransmitters glutamate and GABA had their specific receptor binding increased in most of the brain areas studied, but decreased in some areas. The glial enzyme, glutamine synthetase, had its activity increased in the cerebellar hemisphere following 4 weeks exposure to 1000 ppm. This suggests that glial cells in the area may have proliferated, a frequent phenomenon following CNS damage (Bjornaes and Naalsund, 1988).

22. The acute effects of toluene are due to pharmacological mechanisms that are similar to other CNS depressants such as 1,1,1-trichloroethane. Acute exposure to toluene is associated with anticonvulsant and anxiolytic effects (Bowen et al., 1996; Lopez-Rubalcava et al., 2000) and has discriminative stimulus properties that are similar to those of ethanol (Rees et al., 1987a), pentobarbital (Rees et al., 1987b) and diazepam (Bowen et al., 1999). Suggesting that it like other CNS depressants produces effects in part by modulation of neuronal firing. Toluene and other abused inhalants such as 1,1,1-trichloroethane have been shown to potentiate the function of $GABA_A$ receptors expressed in *Xenopus* oocytes (Mihic et al., 1997; Beckstead et al., 2000).

23. To investigate the effects of acute toluene exposure on the amino acid neurotransmitter levels in the hippocampus, an *in vivo* microdialysis study was performed in freely moving mice after a single intraperitoneal administration of toluene (150 and 300 mg/kg). Amino acid neurotransmitters in microdialysates were measured by a high performance liquid chromatography system. The extracellular levels of glutamate and taurine were rapidly and reversibly increased within 30 min after the toluene administration in a dose-dependent manner and returned to the basal level by 1h. Conversely, the extracellular level of glycine and GABA were stable, and no significant change was observed after the toluene administration. To further investigate the brain toluene level in the hippocampus of toluene-administered mice, a solid-phase microextraction (SPME) method was used and the time course changes of toluene in the hippocampus of living mice were examined. The brain toluene level reached the peak at 30 min after injection and returned to the basal level after 2h and the relationship between brain toluene levels and amino acid neurotransmitter glutamate and taurine levels in the hippocampus was observed. These findings suggest that toluene glutamatergic and taurinergic neurotransmission in the hippocampus of freely moving mice possibly by increasing neurotransmitter release (Win-Shwe et al., 2007).

24. There is also evidence indicating that toluene modulates the activity of ionotropic glutamate receptors. Toluene has also been demonstrated to produce phencyclidine-like discriminative stimulus effects (Bowen et al., 1999), suggesting that it may acutely inhibit *N*-methyl-D-aspartate (NMDA) receptors. In vitro studies using *Xenopus* oocytes transfected with heterologous recombinant NMDA receptors, toluene rapidly and reversibly inhibits receptor function (Cruz et al., 1998). These studies assessed the effects of toluene on the electrophysiological function of NMDA receptors containing NR1 subunits in combination with NR2A, NR2B or NR2C subunits. Of these, the NR1/2B combination was the most sensitive to the inhibitory effects of toluene while other non-NMDA receptor subunits were less sensitive. These studies suggest that toluene may produce some of its effects by directly modulating NMDA receptor function in a subunit-selective manner.

25. The pharmacologic effects of toluene may be inhibitory or excitatory. Of equal concern is the observation that toluene activates signal transduction pathways that regulate expression of GABA and glutamate receptors. Exposure to toluene has been associated with an increase in the incidence of temporal lobe epilepsy and decrease in IQ scores (Byrne et al., 1991). The mechanism associated with these changes in seizure susceptibility and cognitive function appear to involve toluene induced alterations in receptor sybtype expression. Toluene increases expression of the alpha1 subunit of the $GABA_A$ receptor and of the NR1, NR2B and GluR2/3 subunits of the glutamate receptors in the medial prefrontal cortex. Decreased $GABA_A$ alpha1 and glutamate NR1 subunits expression was seen in the substantia nigra pars compacta. Toluene inhalation produced modest increases in $GABA_A$ alpha1 subunits in the striatum, as well as slight decreases in the expression of this subunit in the ventral tegmental area. NR2B subunit levels were slightly increased within the nucleus accumbens by toluene. These studies show that toluene differentially alters the levels of specific $GABA_A$ and glutamate receptor subunits in a regionally selective manner (Williams et al., 2005). These changes in receptor expression can predipopse the individual to seizures and to excitotoxicity. ICR mice exposed to 250 ppm toluene via inhalation for four days developed mild dependence upon termination that was characterized by an increase in severity of handling-induced convulsions (Wiley et al., 2003). The effects of toluene on the sensitivity to seizures induced by aminophylline has also been investigated in mice. Toluene increased seizure susceptibility to aminophylline in a dose- and time-dependent manner. Toluene-induced enhancement of seizure susceptibility to aminophylline occurred as early as 30 min and persisted for at least 3 days after a single administration of toluene (500 mg/kg) (Chan and Chan, 2003). *These observations are extremely important since they indicate that toluene makes neurons more vulnerable to excitation and thus to excitotoxicity.*

26. When a glutamatergic motor neuron dies (irrespective of why it dies) it releases glutamate into the extracellular space. This glutamate is free to act on adjacent motor neurons and cause these cells to experience an increase in calcium influx that ultimately leads to cell death. As each adjacent neuron dies the amount of glutamate in the extracellular space increases. This promotes a vicious excitotoxic cascade that perpetuates the loss of neurons.

27. Compounds that inhibit glutamaterigic neurotransmission are promising candidates as therapeutics for ALS. Unfortunately, the cell's own machinery is genetically predisposed to modulate glutamatergic neurotransmission at a set level for optimum brain function. As a result, the cells quickly override this pharmacologic effect by generating more glutamate receptors, which actually increases the risk of excitoxicity. As a result the clinical efficacy of compounds such as rulizole is limited at best. The recommendation that rulizole not be stopped abruptly once therapy is initiated is related to this phenomenon. Since the cells are naturally trying to combat the effect of the drug, abruptly stopping it

leaves the cells in an up-regulated state and therefore even more vulnerable to the excitotoxic effects of glutamate.

Apoptosis and Toluene

28. *In vitro* and *in vivo* data suggest that decreased GSH promotes multiple apoptotic pathways contributing, at least partially, to motor neuron degeneration in ALS (Chi et al., 2007). It has been shown that the inhalation of toluene in rats can cause neuronal apoptosis in the central nervous system. However, the cellular and molecular effects of toluene directly on astrocytes are not well studied. The following study used primary cultures of astrocytes isolated from the neonatal rat cortex as a model to study the toluene effects on cell outcome and associated signal transduction pathways using immunostaining and Western blotting. Acute toluene exposure significantly induced caspase-dependent cell apoptosis and transiently stimulated the activation of p42/44 mitogen-activated protein kinase (MAPK) in the primary astrocytes. Interestingly, the inhibition of the p42/44 MAPK signaling cascade by PD98059 in conjunction with the toluene treatment evoked more cellular apoptosis than toluene alone, suggesting that the toluene-induced transient MAPK activation may play a role in promoting cell survival during the toluene exposure (Lin et al., 2002).

29. To study the cytotoxicity of toluene and its mechanism, hippocampal neurons were cultured and exposed to toluene *in vitro*. The neurons from newborn SD rat's hippocampus were primarily cultured for two weeks, then administered with toluene (3, 6, 9 mmol/L), with blank control group and excipient group being also set up. 24 hours later, Morphology and viability of the cells, the LDH activity, [Ca2+]i, and cell apoptosis were examined. Protuberances of neurons of the toluene-exposed groups were damaged; the bodies of the neurons became round and swollen; the number of the cells decreased; the LDH activity of neurons of high-dose group increased significantly compared with control group ($P < 0.05$). [Ca2+]i of toluene-exposed groups also increased significantly compared with control group($P < 0.05$) in a dose-dependent manner; after diltizem as antagonist of calcium tunnel was added, no increase of [Ca2+]i was found; and evident apoptosis of the exposed cells were also found. Toluene was toxic to the neurons after being administered *in vitro*, which might be ascribed to higher lipid solubility of toluene and it's ability to increase calcium influx, the latter facilitating apoptosis (Yan et al., 2004).

30. The mechanisms underlying the acute neurophysiological and behavioral effects of volatile organic compounds (VOCs) remain to be elucidated. However, the function of neuronal ion channels is perturbed by VOCs. The present study examined effects of toluene (TOL), trichloroethylene (TCE), and perchloroethylene (PERC) on whole-cell calcium current (ICa) in nerve growth factor-differentiated pheochromocytoma (PC12) cells. All three VOCs affected ICa in a reversible, concentration-dependent manner. At +10-mV test potentials, VOCs inhibited ICa, whereas at test potentials of -20 and -10 mV, they

potentiated it. The order of potency for inhibition (IC50) was PERC (270 microM) > TOL (720 microM) > TCE (1525 microM). VOCs also changed ICa inactivation kinetics from a single- to double-exponential function. Voltage-ramp experiments suggested that VOCs shifted ICa activation in a hyperpolarizing direction; this was confirmed by calculating the half-maximal voltage of activation (V1/2, act) in the absence and presence of VOCs using the Boltzman equation. V(1/2, act) was shifted from approximately -2 mV in control to -11, -12, and -16 mV by TOL, TCE, and PERC, respectively. Similarly, VOCs shifted the half-maximal voltage of steady-state inactivation (V1/2, inact) from approximately -16 mV in control to -32, -35, and -20 mV in the presence of TOL, TCE, and PERC, respectively. Inhibition of ICa by TOL was confirmed in primary cultures of cortical neurons, where 827 microM TOL inhibited current by 61%. These data demonstrate that VOCs perturb voltage-sensitive Ca2+ channel function in neurons, an effect that could contribute to the acute neurotoxicity of these compounds (Shafer et al., 2005)

31. Chronic toluene inhalation at concentrations above occupational exposure limits (e.g., 100 ppm; NIOSH) has been repeatedly shown to induce neurotoxic effects. In contrast, although few clinical and experimental data are available on the effects of toluene exposure at concentrations below occupational exposure standards, some of these data may support adverse effects of long-term exposure to low toluene concentrations. To test this hypothesis, Berenguer et al., (2003) investigated the neurobehavioral and neurochemical effects of 40 ppm inhaled toluene in a rat model of 16-week subchronic exposure, examining locomotor and rearing activities; adaptation/sensitization to narcosis produced by acute exposure to toluene at high concentration; and tyrosine hydroxylase and tryptophan hydroxylase activities, and dopamine (DA) and serotonin (5-HT) turnovers in the caudate-putamen, nucleus accumbens, hippocampus, prefrontal cortex, and cerebellum. The results of this study mainly show that subchronic exposure to 40 ppm toluene resulted in sensitization to toluene-induced narcosis, a decrease in rearing activity, and alterations in DA and 5-HT neurotransmission. *This demonstrates that subchronic toluene exposure at a low concentration may lead to adverse changes in neurobehavioral and neurochemical functioning, and further questions in a public health perspective the actual neurotoxic potential of toluene and other organic compounds, because deficits in functioning are generally viewed as precursors of more serious adverse effects* (Berenguer et al., 2003).

32. Gotohda et al., (2006) from the Department of Forensic Medicine, Institute of Health Biosciences, The University of Tokushima Graduate School, in Tokushima, Japan investigated the effects of toluene inhalation on neurons and neurotrophic factors in the spinal cord and the relationship between them. Male Wistar rats were exposed to toluene (1500ppm for 4h per day) for 7 days. To observe damage of the neurons in spinal cord due to toluene, expression of microtubule associated protein 2 (MAP2) and 70kDa heat shock protein (HSP70) were determined by immunohistochemistry. MAP2 was degraded and HSP70-

immunoreactivity was enhanced in nerve cell bodies of the gray matter in toluene inhalation group. Immunoreactivity of glial fibrillary acidic protein (GFAP), a marker of astrocytes, was enhanced in the toluene-treated group. Furthermore, glial cell line-derived neurotrophic factor (GDNF)- and brain-derived neurotrophic factor (BDNF)-immunoreactivity in spinal cord were slightly decreased in the treated group. In addition, the concentrations of GDNF and BDNF in the spinal cord were determined using enzyme linked immunosorbent assay (ELISA). Concentration of GDNF was reduced significantly by toluene exposure. BDNF also reduced, but not significantly. The toluene inhalation caused damage to neurons in the spinal cord, which was accompanied by a decrease in the neurotrophic factors, such as BDNF and GDNF (Gotohda et al., 2006). MAP2 expression decreased in the anterior gray horn of all ALS cases and in the intermediate gray of several ALS cases. This reduction was correlated with the degree of degeneration and neuronal loss in anterior horn cells and with the clinical symptoms of limb weakness (Kikucki et al., 1999). *These observations provide compelling support for the interaction between exposure to toluene and the progression of ALS.*

33. In summary, I have presented the mechanisms by which toluene is posited to cause the death of neurons. Whenever possible I have provided data related to the effects of toluene on motor neurons specifically. I have defined the necessary terms so the reader can follow the materials presented herein. I have related this material to the mechanisms of neuronal loss implicated in ALS and to the current therapies for ALS specifically for the purpose of demonstrating how chemicals can negatively alter the course of the disease. I have provided an extensive review of the literature to provide the reader with sufficient data to appreciate that toluene exposure is associated with oxidative stress and glutamatergic excitotoxicity both which as described above have also been very strongly implicated in the pathogenesis of ALS.

K. Dan Allen's Level of Exposure to Toluene

1. The Occupational Safety and Health Administration (OSHA) considers toluene to be a toxicant. The current OSHA Permisible Exposure Limit for toluene is 200 ppm TWA; Also, exposures shall not exceed 300 ppm (15 minute TWA ceiling) with the following exception: exposures may exceed 300 ppm, but not more than 500 ppm (peak), for a single time period up to 10 minutes for any 8-hour shift. (29 CFR 1910.1000).

2. According to the OSHA "before a worker is placed in a job with a potential for exposure to toluene, a licensed health care professional should evaluate and document the worker's baseline health status with thorough medical, environmental, and occupational histories, a physical examination, and physiologic and laboratory tests appropriate for the anticipated occupational risks. These should concentrate on the function and integrity of the central nervous system and skin. A preplacement medical evaluation is recommended to assess an

individual's suitability for employment at a specific job and to detect and assess medical conditions that may be aggravated or may result in increased risk when a worker is exposed to toluene at or below the prescribed exposure limit. The health care professional should consider the probable frequency, intensity, and duration of exposure as well as the nature and degree of any applicable medical condition. Such conditions (which should not be regarded as absolute contraindications to job placement) include a history and other findings consistent with diseases of the central nervous system or skin."
(http://www.osha.gov/SLTC/healthguidelines/toluene/recognition.html)

3. OSHA has reviewed the literature and noted the following acute effects of exposure to toluene: "Volunteers exposed to a 200-ppm concentration of toluene for 8 hours experienced mild upper respiratory tract irritation; at 400 ppm, subjects experienced mild eye irritation and tearing and laughed inappropriately; at 600 ppm, the volunteers developed slight nausea and lassitude; and at 800 ppm, they experienced drowsiness, incoordination, and a metallic taste in the mouth [Clayton and Clayton in Patty's Industrial Hygiene and Toxicology, 1981-1982, p. 3283; Hathaway, Proctor, Hughes, and Fischman, Proctor and Hughes' chemical hazards of the workplace. 1991, p. 546]."
(http://www.osha.gov/SLTC/healthguidelines/toluene/recognition.html)

4. Echeverria et al., 1989 noted subtle acute effects to be associated with exposure to toluene at just below (75 ppm) and above (150 ppm) the OSHA PEL of 100 ppm supporting the position that the guideline be lowered since the biological threshold of behavioral effects may be comparable with the TLV. It should be noted the OSHA PEL of 100 ppm was vacated on July 7, 1992, in accordance with the U.S. Court of Appeals, Eleventh Circuit, ruling which vacated the 1989 PELs listed in the "Final Rules" columns of Table Z-1-A of 29 CFR 1910.1000.

5. Mr. Allen and his coworkers reported symptoms that included dizziness, nausea and headaches. Based on these reported symptoms and the results of the findings reported in the studies cited by OSHA, Mr. Allen had to have been exposed to concentrations that at least exceeded the OSHA PEL, established to protect workers against the health effects of exposure to hazardous substances. In addition, Mr. Allen who we now know had latent ALS at the time of his exposure did not receive medical clearance before he was exposed to toluene and other chemicals used in the floor refurbishment process as recommended by OSHA. (http://www.osha.gov/SLTC/healthguidelines/toluene/recognition.html)

L. My Case Specific Causation Assessment

I have used the data presented herein to formulate my conclusions regarding causation in this case. To arrive at this conclusion:

1. I first compiled a list of acute complaints and symptoms and related these chronologically to all possible occupational and non-occupational sources of chemical exposures.

2. I have noted the time of onset, duration, and intensity of the acute complaints and indicated when symptoms worsen or remit in relation to exposure (e.g. work week, week end, time of shift, on vacation).

3. I have evaluated Mr. Allen's family/genetic health, special sensitivities, and possible congenital factors.

4. I have identified the chemicals Mr. Allen was exposed to and how these were used.

5. Whenever possible, I have obtained chemical names (not trade label names), material safety data sheets, and other identifying data concerning each substance.

6. I have reviewed the workplace information provided regarding ventilation systems and floor plans.

7. I have attempted to obtain environmental and industrial hygiene air measures to prove the presence of alleged chemicals in the alleged source.

8. I have attempted to obtain urine and/or blood samples from the affected individual to establish body burden of chemical. Although these measures were not available in this case, there is nevertheless sufficient evidence based on acute symptoms of exposure reported by Mr. Allen and others along with the documentation of the events to conclude that a substantial exposure to the chemicals identified did occur.

9. I have obtained information on dose-response relationships, animal studies, toxicological and epidemiological studies for the chemicals cited.

10. I have confirmed the subject's complaints by a clinical neurological examination, neurophysiological tests, and, appropriate blood and urine analyses.

11. I have differentiated these findings from those seen in idiopathic primary neurological disease.

12. I have attempted to find alternative explanations based on the findings of past medical history, previous and/or current unrelated exposures to substances from sources other than the one under consideration.

13. I have identified and critically reviewed previously published and/or reported case reports, case control studies, population studies, and animal studies concerning the alleged neurotoxicants and related this to the case specific data.

14. I have considered all of this information collectively in arriving at my opinion. It is my professional opinion based on my training and experience that there is sufficient data in this case to arrive at the following conclusions with a reasonable degree of scientific certainty.

M. Conclusion

1. ALS is a progressive neurodegenerative disorder associated with loss of motor neurons that is mediated by in part by oxidative stress and in part by glutamate mediated excitotoxicity which collectively lead to cell death via induction of apoptosis (programmed cell death). These two mechanisms each play important roles in the onset and progression of the disease.

2. Mechanisms that prevent either oxidative stress or glutamate mediated excitotoxicity are useful in delaying the onset and slowing the progression of ALS in both animal models and in humans.

3. It logically follows that exposure to chemicals that increase oxidative stress or glutamate-mediated excitotoxicity will hasten both the onset and the clinical course of ALS. Furthermore, a researcher would have to ignore the scientific method of reasoning to hypothesize otherwise.

4. Mr. Allen and his coworkers reported exposures to chemicals at concentrations that were at least high enough to cause acute symptoms including dizziness, nausea and headaches.

5. It can therefore be concluded with a reasonable degree of medical certainty that the exposures were high enough to alter neuronal functioning since dizziness is a symptom of this.

6. My review of the materials provided indicates that

- Mr. Allen was exposed to neurotoxic chemicals during the refurbishment of the gym floor;
- Mr. Allen's experienced symptoms consistent with disruption of normal neurological function during his exposure;
- Mr. Allen developed symptoms of ALS in chronological relationship to this specific exposure event;
- Mr. Allen had no family history of ALS which typically develops earlier in life than sporadic ALS but also runs a slightly longer course (According to a report by authors from the Laboratory of Central Nervous System Studies, National Institutes of Health, the age-dependent incidence of sporadic ALS, the age of onset of familial ALS is normally distributed about a mean of 45.7 years-old (Strong et al., 1991; Norris et al., 1993); and 5) that his first overt symptoms of ALS emerged when he was only 45-years-old.

7. ALS is general considered to be a disease of middle to late life. Published reports indicate that the average age at onset for non-familial sporadic ALS is 60 years-old (Sorenson et al., 2002; Norris et al., 1993; Juergens et al., 1980).

8. These observations indicate that Mr. Allen developed the disease much earlier than would be expected based on his negative family history and the epidemiological findings (Sorenson et al., 2002; Chio et al., 2002).

9. There is also sufficient evidence to support the conclusion that the exposure to Toluene and other chemicals was a substantial contributory factor in the age at onset of the disease since there was no reported family history of the disease, the age at onset was atypical, the onset occurred after the exposure event, and several of the chemicals Mr. Allen was exposed to are known to be neurotoxic (e.g., toluene).

10. It can therefore be concluded with a reasonable degree of medical certainty that Mr. Allen would have been unlikely to develop overt symptoms of ALS at age 45-years-old and would not have died on May 16, 2004 had he not been exposed to the chemicals used in the gym floor refurbishment process.

11. I hold all of the opinions in this report to a reasonable degree of scientific certainty. I reserve the right to further supplement this report and respond to the reports submitted by the defense.

Marcia Ratner, Ph D.

Dated: June 14 2007

EXHIBIT E 1

COMMONWEALTH OF MASSACHUSETTS

DISTRICT OF MASSACHUSETTS

****

LAURA ALLEN, INDIVIDUALLY; And As ADMINISTRATRIX OF THE ESTATE OF DANIEL ALLEN; And AS NEXT FRIEND OF TAYLOR ALLEN AND DANIELLE ALLEN; And MARK ALLEN,

Plaintiffs

vs. No. 05-40048-FDS

MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES; SOUTHWEST RECREATIONAL INDUSTRIES, INC., d/b/a MARTIN SURFACING,

Defendants

****

VOLUME: I

PAGES: 1-203

DEPOSITION of MARCIA H. RATNER, Ph.D.

Tuesday, August 7, 2007

10:00 a.m.

Offices of Mullen & McGourty

52 Temple Place

Boston, Massachusetts

Megan McGovern Williams, Court Reporter

APPEARANCES:

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EXHIBITS

PROCEEDINGS

(Before the commencement of the deposition, the following exhibits were marked:

(Four-page curriculum vitae of Marcia Hillary Ratner, Ph.D. marked exhibit 1 for identification.)

(Opinion marked exhibit 2 for identification.)

(References marked exhibit 3 for identification.)

(Four-page Affidavit of Robert Bradley marked exhibit 4 for identification.)

(Three-page Affidavit of Paul Bachia marked exhibit 5 for identification.)

(Three-page Affidavit of Paul Crecelius marked exhibit 6 for identification.)

MARCIA H. RATNER, Ph.D., first having been satisfactorily identified by the production of her driver's license and duly sworn by the notary public, testified under oath as follows in answer to direct examination by MR. MAHONEY:

MR. MAHONEY: We are going to have the usual stipulations. All objections except as to form will be reserved as will motions to strike. We will give the witness 30 days from completion of the deposition testimony to review the transcript for accuracy. We will waive notarization.

Anything else, James?

MR. GOTZ: That is it.

MR. MAHONEY: We have premarked the following exhibits: Doctor Ratner's CV is number 1. Her opinion is number 2, and that is pages 2 through 33. The references referred to in the opinion were marked as exhibit 3, pages 34 through 41. The Bradley affidavit is exhibit 4. The Bachia affidavit is exhibit 5, and the Crecelius affidavit is exhibit 6.

BY MR. MAHONEY:

Q. Would you please state your name for the record?
A. Marcia Ratner.
Q. Where do you live?
A. My address at home is 24 Livesey, L-I-V-E, Road in Squantum, Mass.
Q. 02171?
A. That's right. You are from Quincy, too?

Q. I grew up in Wollaston.

Can you give me a thumbnail sketch of your educational background commencing with college graduation?

A. I graduated from Boston University in 1995 with a bachelor's in psychology and premed requirements fulfilled. I graduated from Boston University School of Medicine in 2004 with a Ph.D. in human behavioral neuroscience. And I finished a three-year postdoctoral, NIH-sponsored fellowship in 2007.

Q. What was the concentration of the fellowship?

A. Aging.

Q. Are you licensed to practice medicine in the Commonwealth of Massachusetts?

A. No. I do not practice. I just do research.

Q. Are you licensed to practice medicine in any state in the United States?

A. No. Again, I only do research.

Q. Are you licensed to practice medicine in any country?

A. No.

Q. And can you explain your employment background, please, since your graduation from Boston University

Medical School?

A. I have worked for the department of pharmacology at Boston University School of Medicine in the capacity of project manager for a laboratory as a molecular neurobiologist.

Q. What were your duties in that position?

A. I did research in in vivo studies to develop new drugs for treating for neurodegenerative diseases and psychiatric disorders.

Q. For a neuro what?

A. Neurodegenerative diseases and psychiatric disorders.

Q. How long have you held that position?

A. Three years.

Q. And you graduated from Boston University School of Medicine in 2004?

A. Um-hmm. I ran and did the fellowship consecutively while being project manager for the lab while doing my fellowship because I was taken in in that capacity because of past experience as a project manager. It is unusual for a postdoctoral fellow to be offered that position, but.

Q. Now have you ever met Dan Allen or had you ever met Dan Allen?

A. I saw him in clinic with my colleague, Joe Jabre.

Q. Doctor Jabre, is he licensed to practice medicine in the Commonwealth?

A. Yes.

MR. MAHONEY: Let's go off the record.

(Brief discussion off the record.)

MR. MAHONEY: On the record.

BY MR. MAHONEY:

Q. When you say you saw him in a clinic, what type of a clinic was that?

A. We have an occupational and environmental neurology program with the department of neurology at BU School of Medicine. I was the project manager and continue to be the project manager for that program.

At that time, we were consulted to see him. He was brought into the office, and we checked him to ascertain a diagnosis of his neurological symptoms.

Q. When you say you consulted to see him, who consulted you to see him?

A. I think we were originally contacted by Attorney Alan Bell.

Q. From Florida?

A. I think he was from California. I think.

Q. So when you saw Mr. Allen, Coach Allen, it wasn't for the purposes of providing him with any treatment; is that fair to say?

A. That is fair to say.

Q. When did you see Coach Allen? Do you remember exactly?

A. It probably was 2004.

Q. And you understand that he has passed?

A. Yes.

Q. Do you have a memory of when your exam took place in conjunction with his passing?

A. It was before, obviously. He passed away very close.

Q. Months?

A. Months. Like I remember that he passed away within a very short time after we saw him. In fact, it was surprising how fast he was gone, although by the time we saw him, he was quite symptomatic. He had bulbar signs at that point and was starting to really get pretty bad. He was in pretty late stages of the disease when we saw him.

MR. MAHONEY: I have a letter to Agnelli which was signed by Doctor Ratner and Doctor Jabre, so I will mark that as the next exhibit.

(Three-page letter from Joe Jabre, M.D., and Marcia H. Ratner, Ph.D., to Attorney Joseph Agnelli dated December 5, 2005 with attachments marked exhibit 7 for identification.)

BY MR. MAHONEY:

Q. Have you ever testified in a legal matter prior to today's deposition?

A. No.

Q. Have you ever been deposed before?

A. No.

Q. Had you ever worked with Attorney Alan Bell prior to him asking for your consultation in Mr. Allen's case?

A. No.

Q. Had you ever worked with Attorney Agnelli prior to this matter?

A. No.

Q. The clinic that you say you are the project manager of at BU, the occupational and environmental neurology program, does that treat patients?

A. We generally -- unfortunately, with most toxicant-induced neurosystem damage, there is very little treatment. So most of the work we do is

simply for diagnostic purposes of ascertaining causation.

So we get a lot of referrals either from physicians who aren't sure about a diagnosis from around New England and all over the world, actually, and also from attorneys who may have legal cases occasionally when they have questions as well about causation.

Q. You have provided a written opinion with regard to causation of Mr. Allen's illness in this case; is that right?

A. Um-hmm.

MR. GOTZ: You need to say yes or no.

A. Yes.

Q. Have you ever provided a written opinion in any other legal matter regarding causation of any type of neurological problem that existed in a person that you saw?

A. Yes.

Q. How many other times?

A. Probably half a dozen.

Q. And when you provided an opinion in these cases, was it an opinion that you provided in conjunction with Doctor Jabre?

A. Sometimes; sometimes not.

Q. The other half a dozen times that you provided an opinion, were they ever used in a courtroom setting that you are aware of?

A. I really don't know for sure. I know that those cases settled.

Q. Have you ever testified at the Department of Industrial Accidents in Massachusetts?

A. Not that I am aware of.

Q. The opinion that we have marked as exhibit 2, this was authored by you; is that right?

(Handing exhibit 2 to the witness.)

(Witness viewing exhibit 2.)

A. Yes. This appears to be my report.

Q. And Doctor Jabre didn't write this opinion; is that right?

A. No.

Q. You said no?

A. No.

Q. Do you happen a have a copy of this available to you? If not, you can look at this because I have got another one here.

(Handing document to the witness.)

Q. I am looking at page 32, and I would ask you to turn

to page 32.

(Witness complying.)

Q. Paragraph, 5 you can tell me if I read this correctly.

"It can therefore be concluded with a reasonable degree of medical certainty that the exposures were high enough to alter neuronal functioning since dizziness is a symptom of this."

A. That is correct.

Q. You testified a few moments ago that you are not a medical doctor; is that right?

A. I do not practice, no.

Q. So that you are not qualified to offer an opinion with regard to a reasonable degree of medical certainty; isn't that fair to say?

A. I am not sure. I was trained at Boston University School of Medicine in human behavior and neuroscience. I was trained to do a neurological exam in the course of that education, and I did rotations in clinic and in the Department of Neurology at Boston University School of Medicine. I have seen patients with symptoms with dizziness and other symptoms, and I have been trained to understand the vestibular system and its

relationship to those symptoms.

So I think I am qualified to offer, with a reasonable degree of medical certainty, how that system functions. If you want to know from the perspective of whether I offer treatment for that, no. But can I define whether or not that in fact was the case? Yes. I think I am qualified to state that.

Q. You have never take the medical boards; is that right?

A. No. As I said, I don't practice. Boston University offers two degrees, the Ph.D. and the M.D.

Q. And you chose the Ph.D.?

A. I chose the Ph.D. because I decided that I wanted to do research.

Q. You are not a board-certified neurologist; is that right?

A. No. I am a behavioral neuroscientist. I am trained in how the nervous system affects behavior.

Q. Behavioral neuroscience rather than a practicing physician; is that right?

A. That is correct. I do not practice. The M.D. is a professional degree. The Ph.D. is a scientific research degree. Actually, the M.D. is the lower

degree.

Q. With that in mind, I would like you to explain the difference that you detail in paragraphs 10 and 11. In paragraph 10, you say, "It can therefore be concluded with a reasonable degree of medical certainty that Mr. Allen would have been unlikely to develop overt symptoms of ALS at age 45 years old and would not have died on May 16, 2004 had he not been exposed to the chemicals used in the gym floor refurbishment process." Yet in paragraph 11, you say you "Hold all of the opinions in this report to a reasonable degree of scientific certainty."

A. Um-hmm.

Q. Why in paragraph 10 and in paragraph 5 do you conclude your opinions with a reasonable degree of medical certainty, whereas in paragraph 11, you say you hold all of the opinions expressed above with a reasonable degree of scientific certainty?

A. As I stated before, the medical degree is a professional degree to practice medicine. It is not an academic degree. It is not as high a degree as a Ph.D. My opinions offered in here have both scientific, which underpin all of medicine, and medical value.

From a practicing position of diagnosing the condition of ALS, it is a medical certainty. But from a mechanistic standpoint, the scientific certainty in those mechanisms contribute directly to the clinical manifestations. Otherwise, you wouldn't have them. So you have to go back to the science in order to support the behavior.

Behavior does not exist and cannot be understood without the science, so science still overrides the practice of medicine because that defines how the body works, not just the diagnostic procedure followed by a physician in practice.

Q. What do you mean when you say that a Ph.D. is a higher degree than a medical degree?

A. The Ph.D. is a academic degree. It is similar to a J.D. The J.D. is a professional degree. The M.D. is a professional degree and is not an academic degree.

A scientist doing research in medicine is trained specifically to do a type of scientific research as it pertains to medicine. So if you are studying pharmacology or if you are studying neuroscience or if you are studying any other aspect of systems function, you are looking at and writing

the medicine. It then becomes the practice of medicine.

Most physicians do not do research. They practice medicine. They do not develop medicine. They oftentimes will work in the capacity, because of their license, to facilitate the development of drugs for use in human populations, but they do not define by their work how the systems work, how the body works, and they don't typically write the books from which they all are trained. In fact, your first two years of medical school are primarily taught by people with Ph.D.s who then -- you do your second two years of your rotations where you learn how to deal with patients. And then you do a residency, which then, in my opinion, is where you become a doctor. You learn to specialize in an area, and you get board certified in an area of expertise, narrowing down your focus and really securing your education as an expert in a specific area.

MR. GOTZ: Just a reminder to wait for the question to be completed before you start answering.

A. Um-hmm.

Q. When you got your doctorate of philosophy, what did

you write your thesis on?
A. Parkinson's disease, age of onset, and its relation to chemical exposures.
Q. Is Parkinson's disease similar to ALS?
A. It is a neurodegenerative disease as is ALS, yes.
Q. What similarities do the two diseases enjoy?
A. Both disease are associated with loss of neurons in the central nervous system.
Q. And how is Parkinson's manifested?
A. Parkinson's -- the clinical manifestation of Parkinson's includes bradykinesia, cognal rigidity, tremor. And these symptoms are related to the loss of dopaminergic neurons in the substantia nigra pars compacta.
Q. Are a patient's cognitive abilities affected by Parkinson's?
A. Generally, it is not to a large extent, but there are some behavorial manifestations that have been reported in the literature.
Q. And what are the manifestations of ALS?
A. The ALS manifestations are motor system dysfunction. Patients will have fasciculations of muscle fibers and eventual loss of motor control. This may start with bulbar presentation or may start from the

presentation in the extremities, generally progressing ultimately to a loss of respiratory function and death.
Q. Are there cognitive losses associated with ALS?
A. Generally, it is considered that there are. Again, the lesion is confined primarily to motor neurons, which are the glutamatergic neurons that protect the motor cortex in the case of the upper motor neurons.

And then the lower motor neurons project to the extremities, and it is these lower motor neurons that are primarily affected in ALS.
Q. What are some of the symptoms of Parkinson's that are not manifest in a person who has been diagnosed with ALS?
A. You wouldn't see cognal rigidity; you wouldn't see bradykinesia; you wouldn't see the tremor that you see in Parkinson's. And conversely --
Q. That is my next question, actually.
A. Conversely, you wouldn't see the paralysis in Parkinson's as you do in ALS.
Q. Anything else?
A. You know, the pathology is clearly grossly different, so if you examine the brain, if you examine the spinal cord, you would see the frank

pathological differences I already discussed.
Q. Could you just repeat them, the frank pathological differences between the two diseases?
A. Well, Parkinson's disease is affecting dopaminergic neurons, and ALS is affecting motor neurons. So one is involving primarily dopamine; the other is involving primarily glutamatergic neurons.
Q. We will be discussing your opinion in detail, but what I want to ask you about now are some general questions about it. Has your opinion as you have expressed it in this case ever been peer reviewed?
A. This particular opinion --
Q. Yes.
A. -- in this case? I have a book chapter on age of onset in Parkinson's disease in one of the latest Parkinson's books.

I have a peer-reviewed publication that I wrote with Bob Feldman in 1999 talking about age of onset of neurodegenerative disease. That was peer reviewed in the current opinion in Neurology.

So those are -- that Parkinson's book was reviewed by every expert in Parkinson's disease in this country that contributed to it. So although it is not a chapter or an article in a publication,

considering the roster of people who are authors in that book, I was held in very high regard alongside Charlie Canner and William Langston and others in the field, who are my peers.
Q. But this specific opinion, has it been peer reviewed?
A. This has not. Not that I know of.
Q. And the opinion that you said had been peer reviewed related to a Parkinson's study?
A. Um-hmm.
Q. And it is not your opinion that Mr. Allen suffered Parkinson's, is it?
A. No, it is not, but I will qualify that. The factors that contribute to the progression of the disease, the neurodegenerative disease, whether it be Parkinson's disease or ALS, as they interact with loss of neurons induced by toxic exposure are directly the same.

For simplicity reasons, if you lose one neuron in a day due to a neurodegenerative disease and one neuron a day due to a toxic exposure, you have now lost two rather than one. So you are hastening the progression of the disease if you have the two happening in the same person. And therein

lies the problem with the environment interacting with the neurodegenerative disease.

Q. When you talk about a toxic exposure, what diagnosis are you referring to?

A. Are you talking -- you can define -- the only difference between toxicity and treatment using a drug is dose.

In fact, if the drug causes a desirable manifestation, we consider it a treatment. If it causes an undesirable manifestation, we consider it a toxin.

So, for example, enhancing dopaminergic neurotransmission in a patient with Parkinson's disease may afford an increase in movement that would be desirable, but enhancing dopaminergic neurotransmission in a patient with schizophrenia could further exacerbate those problems and be undesirable.

So you have to be very careful when you are choosing a drug or exposing someone to the chemical. You have to consider that context of which that chemical is being used. The pharmaceutical industry grapples with this all the time.

So, you know, this is the --

Q. But when you refer to the loss of a neuron relating to a toxicity, am I wrong in inferring that you are taking about a toxic exposure that caused the loss of the neuron?

A. Can you repeat that?

Q. You referred to -- you compared the loss of a neuron due to, I suppose, degenerative process with the loss of the neuron due to a toxic chemical, is that right, and you said it hastens the loss of the neuron? Is that right? Yes or no.

A. Toxic exposure can cause a loss of a neuron.

Q. Okay.

A. And a neurodegenerative disease can cause the loss of a neuron.

Q. Okay.

A. The toxic exposure can interact with a neurodegenerative disease to hasten the course of the disease. It can make the neuron die sooner, or it can make more neurons die.

Q. What types of toxic exposures have been studied and peer reviewed and published that support what you just said?

A. What -- rephrase that.

MR. MAHONEY: Could you read that back, please?

(The prior question was then read.)

THE WITNESS: Well, there is a recent publication that just came out of Boston University looking at the interaction between Parkinson's disease and herbicides and, in particular, the intersection of this with other genetic polymorphisms to cause a younger onset of Parkinson's disease. That was just published by my colleagues in the department of neurology.

BY MR. MAHONEY:

Q. Did that study conclude that the exposure to herbicides caused Parkinson's?

A. Now, this is very important. I have never said in any of my statements here that neurodegenerative disease is caused by any toxicant. I only have stated that the toxicant can interact with the neurodegenerative disease to hasten its course. In fact, every publication I have ever written follows that same line of reasoning. I have never, ever stated otherwise. And I would be hard pressed to get me to state otherwise, because we don't know what initiates the cascade of a neurodegenerative disease.

Q. Caused by toxins?

A. No. Toxins kill cells. That is why they are called toxins.

A neurodegenerative disease is an idiopathic process that, as far as we know, spontaneously initiates. But this interacts with toxicants, which also kill cells, to hasten the progression of the disease.

So there is no causation here. There is facilitation. There is hastening. There is aggravating, but there is no causation.

Q. Are you familiar with the phrase "multiple chemical sensitivity"?

A. Yes.

Q. You understand that that is not an accepted diagnosis for a neurodegenerative disease?

A. That's correct.

Q. You agree with that?

A. That's correct.

Q. You are not saying in this case that Mr. Allen's exposures to the alleged toxins that were present at Holy Cross is what caused ALS; is that right?

A. I'm sorry. Say that again?

Q. You are saying that the alleged exposures that

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Mr. Allen suffered while he was employed as the Holy Cross football coach are what caused the ALS?
A. No. I would never say that.
Q. You are saying that the ALS in Mr. Allen's case was subclinical, and that when he was exposed to these toxins, it hastened his demise; is that right?
A. That's correct.
Q. What history did you obtain from him to support your conclusion that ALS was subclinical in him prior to his exposure, alleged exposure, at Holy Cross?
A. He had to -- from every report we have, from his own reports, his wife's reports, people who knew him who saw him, you know, around, in reports that I have read, no one indicated ever that he was having -- in fact, some of his physicians who had seen him, too -- that he was having an overt clinical manifestation prior to his exposure to these chemicals. By all accounts, he was healthy prior to that.

So it is certainly reasonable to assume because he had ALS that he had subclinical ALS at that point because the loss of neurons has to be pretty substantial because the manifestations are overt.

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Q. Why is that reasonable to assume when you said a minute ago that no one understands what causes a neurodegenerative disease?
A. When someone is predisposed to a neurodegenerative disease, they are walking around carrying this inside them. It is going to emerge at some point in time in their life.

Typically, ALS emerges somewhere late in life, around 60 years old, and the patient, you know, eventually goes on to die.

Because we have already said we have no evidence whatsoever that ALS is caused by toxic exposure, we don't know what causes ALS, but we know that there are familial forms of ALS. It can be passed on from one family member to another. So we know that people carry the disease and that it emerges later in life.

We know that there has to be substantial loss of neurons before the manifestations become overt. So the first neuron or two that are lost, the patient doesn't necessarily -- is not symptomatic at that point. It is later in the disease as more neurons are lost that the problems start to emerge as being clinically overt.

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Prior to that, there may be changes that are subclinical. If you were to look pathologically at someone who died, you might be able the find evidence that they had subclinical ALS. But you probably wouldn't do that because there would be no suspicion to go look for that at that point.
Q. I want to get back to that last point, but you talked about familial forms of ALS?
A. Um-hmm.
Q. And there is another type of ALS, isn't there?
A. Sporadic.
Q. And Mr. Allen's family history indicated no familial forms of ALS; is that right?
A. That as far as everyone knows, there is no family history. That is correct.
Q. So would you agree that -- well, first of all, do you agree with the diagnosis that he had ALS?
A. I absolutely agree that he had ALS. I saw him, and he definitely had ALS. He had bulbar signs by the time I saw him.
Q. All right. So given that there is no indication in his history of any familial ALS, would you agree that the diagnosis of his ALS condition was sporadic?

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A. I would agree.
Q. You said a moment ago that there aren't any studies -- and I think I am paraphrasing because I don't have your education -- but I think you said that there are no studies of subclinical ALS patients because there is no reason, basically, to look at these people; is that right?
A. Right.
Q. So you are saying that -- well, let me ask you this.

When in Mr. Allen's case --

MR. MAHONEY: Strike that.

Q. Have there ever been any studies that suggest when ALS afflicts a person whether it is subclinical or overt?
A. Well, I mean in general it is believed that ALS emerges in the sixth decade, late in life.
Q. Those are the overt symptoms?
A. Right.
Q. So have there been any studies that you are familiar with that have researched when those people who have the overt symptoms acquired the first -- I don't want to say "signs," because it is not going to look subclinical -- but acquired ALS, acquired a predisposition to ALS?

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A. I think what you are asking, if I understand it correctly, is unanswerable. You wouldn't know they had it, so how would you go look for it? You wouldn't know who to single out. You wouldn't have any, you know, reason. I mean you have to know someone has the disease or a suspicion of the disease.

Now you could, you know, possibly look at people with familial ALS and study them longitudinally and follow them. I don't think that there is any indication that that type of study has been done. It would be expensive and time consuming.

So, you know, if there is such a study, that could ascertain that, but I am not aware that there is such a study at this point.

MR. GOTZ: Could we go off the record?

MR. MAHONEY: Sure.

(Discussion off the record.)

MR. MAHONEY: On the record.

BY MR. MAHONEY:

Q. I want to stick with the subclinical issue for a few more moments, Doctor Ratner. I think we have agreed that the diagnosis of ALS in Mr. Allen was not

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familial; is that right?

A. That's right.

Q. So for the rest of the deposition, if you answer my questions, I will assume that you are answering those related to ALS based upon a sporadic diagnosis, and I will make sure I ask all my questions based on a sporadic diagnosis. Is that okay with you?

A. That's fine.

Q. What I am trying to understand is we have the floor refinishing process at Holy Cross in 2001, and prior to that, Mr. Allen had no symptoms of ALS. I am trying to determine when he was subclinical.

Was he subclinical prior to 2001, prior to the floor refinishing process? Was we subclinical at some time after the floor refinishing process, in your opinion?

A. In my opinion, he had began to complain about symptoms with dizziness and other symptoms during the floor refinishing process. His health pretty much from that point forward doesn't seem to have really stabilized. He had some acute viral infections or bacterial infection at some point, but he seemed to ever since that point not experience

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the quality of life that he had prior to that. It seems that, you know, that his progression from that point into the fall of 2001 and forward doesn't, you know, doesn't show that he is getting better and clearing.

Other people who were in that environment during the time of the floor refinishing reported experiencing dizziness and these symptoms and other things, but these passed and nothing else seemed to follow in their case. And that is not surprising in someone who did not have a neurodegenerative disease that was subclinical. You would expect them to recover fairly well with no sequelae.

It is in fact recognized by OSHA that people who have neurodegenerative disease should not be exposed to toluene. So it is considerable to recognize that this interaction probably was the straw that broke the camel's back, so to speak.

Q. So you say he was subclinical prior to the floor refinishing process of May, June of 2001?

A. From everything we can find in his history, I don't see anything that was suggesting that he was having problems that he was seeking attention for prior to that.

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Q. But if there is no way it determine whether a person is subclinical or not, how do you know that he was subclinical prior to May or June of 2001?

A. Because he developed ALS, and people who are predisposed to develop ALS would, as I said, be carrying this. And so we know he was going to get the disease. And we know that this disease process, you know, emerged in short chronological relationship to his exposure. So that cascade following the course of progression of ALS had to be very, very close, very, very close. It would be, you know, just when you consider the rate with which ALS typically progresses from subclinical to clinical and even through its clinical stages, the process would be, you know, latent and then unmasked.

The problem is that as the glutamatergic neurons die and release their glutamate, they hasten the course of each other. It is like a self-fulfilling prophecy. It just gets worse and worse as it progresses, and that is why it is such an aggressive disease because the glutamate actually causes more neurons to die very rapidly once it is released. So the few neurons that are dying early

on, as the cascade takes off, it just snowballs.
Q. He was diagnosed by two medical doctors with ALS; isn't that right?
A. I have seen Doctor Jabre's diagnosis of him, and there were reports prior to Doctor Jabre and I seeing him when that was concluded.
Q. I am talking about his treating physicians.
A. His treating physicians, one of which prescribed Riluzole for him.
Q. Right. One diagnosis occurred at UMass Medical Center, is that right, and the other at the Lahey Clinic in Burlington?
A. I would have to see the reports to remember exactly where they were from.
MR. MAHONEY: Off the record.
(Discussion off the record.)
MR. MAHONEY: Okay. Back on.
BY MR. MAHONEY:
Q. So it was Doctor Chad at UMass Worcester, is that right, who first diagnosed him with ALS?
A. Again, I would have to see reports to see where he was at that point.
Q. Is it your understanding based upon the history that you took from Mr. Allen that he sought a second

opinion with Doctor Russell at the Lahey Clinic?
A. Yes. I think there was more than one opinion sought. I don't think people want to accept a diagnosis of ALS. His wife was a nurse. She was, I think, very reluctant to accept her husband having ALS. She fully understood what would happen if he did.
Q. You said a moment ago that he was carrying this. What did you mean by "carrying this"?
A. Well, we don't know what causes ALS, as I have already said, but we know that he developed it. And we know that certain factors are involved in the progression of ALS. So by virtue of the fact that he developed it in such close chronological relationship to this exposure, and you consider the progression in which the neurons die and how long ALS proceeds in the clinical course, and how long it would take to go from subclinical to clinically overt, I think that it would be improbable that he was not having subclinical ALS at that time. That would imply that the disease would have to be progressing much more slowly.
Q. That is not what I am asking. I wanted you to define -- I am beyond your opinion with regard to

the subclinical opinion that you have.
What I wanted you to define is what you meant by "carrying this."
A. Well, we know he had ALS because he went on to die from ALS. So we know, even though he had no family history of the disease, that he ultimately had ALS. So the necessary ingredients were there in him.
Q. What are the necessary ingredients?
A. Well, what we know about ALS is that it is associated with a loss of glutamatergic neurons. These glutamatergic neurons, when they die, release their glutamate, which causes excitotoxicity in adjacent glutamatergic neurons, which also causes them to die. We also know that oxidative stress is involved.
So we know what causes ALS to progress. What we don't know is exactly what causes those first few neurons to start dying. That trigger has not been identified.
Q. So how do you know he was carrying this if you can't identify the trigger?
A. Well, he developed it, and in very close chronological relationship to the exposure. Within months, he had overt symptoms.

So you would have to -- ALS has to go from subclinical to clinical by a loss of neurons. We see in toxic exposures where people are exposed to chemicals, we call it sometimes a coasting effect, where the disease is initiated, still subclinical, the patient leaves the exposure, and then weeks later, months later, starts to have overt systems because that cascade is going on in the body, still subclinical.
So based on our understanding of that, we can conclude that these processes are ongoing. We can't say exactly when they start, but we do know that they can remain progressing along at a pace, which becomes, as I have already said, more aggressive as the disease gets later and later in its course and the symptoms are worse and worse.
So early on, if you have lost one glutamatergic neuron and it releases its small amount of glutamate into the synapse, that excess glutamate is a very small amount. But as more and more glutamatergic neurons die, there is more and more glutamate around to cause more glutamatergic neurons to die, and the rate progresses.
That is why we use Riluzole to try to treat

it. We want to stop that cascade. We want to block that glutamatergic excitotoxicity to slow the disease down from its relentless, aggressive course.

Q. You keep referring to the exposure that he allegedly endured while he was employed Holy Cross and then the overt symptoms that developed after that. But you are clear -- and I just want to make sure of that -- that it not the exposure that caused the ALS?

A. No. Exposure does not cause ALS. It could only aggravate that glutamatergic and oxidative stress cascade that is the underpinning, mechanistically, of ALS.

So it could not cause it, but what it could do is it could interfere with the body's ability to handle that excitotoxic cascade by either itself increasing the oxidative burden or interfering with the body's ability to scavenge free radicals or by enhancing glutamatergic neurotoxicity by modifying the machinery within the cell and making it more susceptible to glutamatergic excitotoxicity.

So what it does is it interacts with a process that is already there to modify it, in this case, unfortunately, unfavorably. In the case of

Riluzole, which inhibits glutamatergic neurotransmission, more favorably. As I said, if I gave you Riluzole and it was inhibiting glutamatergic neurotransmission, you probably wouldn't want that. But if you are someone who is at risk of dying from a disease, there may be subtle side effects that you are willing to accept to slow that progression by toning down that excitotoxic cascade.

Q. Are you saying that the drug that he was prescribed to treat ALS also hastened his demise?

A. Doesn't contribute, no. Actually, that drug is designed to do the opposite. That drug is designed to slow that cascade of --

Q. And did it in this case?

A. You know, the sad thing about Riluzole and the sad thing about toxicants is it is much more difficult to put the brakes on the snowball coming down the hill than it is to add mass to it.

And, you know, every single thing we do contributes to that mass in our body. It is part of the process of aging. In a person with neurodegenerative disease, that is just magnified. They are already susceptible to that. And stopping

it -- we are working very hard. In fact, I do research in this area myself, on discovering new compounds that can effectively arrest this process.

But we are faced with a lot of things, because people have -- you want to arrest it when it is subclinical, but we are not diagnosing people when they are subclinical, so we can't give them that drug early enough to really slow the progression. And by the time we give them it, it is very late in the clinical course when they already have overt symptoms.

By that point, the glutamatergic excitotoxicity, the oxidative stress is so aggressive that the effectiveness of the drug is really curtailed dramatically. You really want to be giving these things very early on. So that is what medicine is working towards, developing the biological markers so we can diagnose these people earlier and get these treatments into them sooner. But we haven't reached that point.

Q. Who wrote the letter to Attorney Agnelli dated December 5, 2005?

A. That was written in collaboration with my partner.

Q. Doctor Jabre?

A. Doctor Jabre and I.

Q. And the opinion as expressed in that letter, do you stand by it today?

A. Could I read that just to be sure before I say that?

Q. Sure. I am referring to exhibit 7.

(Handing exhibit 7 to the witness.)

(Witness viewing exhibit 7.)

A. Yes. I mean the wording is not as eloquent as I would like, but it basically is.

Q. So you stand by the opinion that is expressed in the three-page document authored by Doctor Jabre and you; is that right?

A. Yes. I would just like to have that last sentence be a little more clear in that it is the age of onset that we are talking about. I think it leads in, but I want to make it clear that that is my opinion. And the language is not concise there, but that is what should be interpreted.

Q. The only time that you met with or saw Coach Allen was prior to writing this report; is that right?

A. That's correct.

Q. And did you have -- what medical records did you have when you authored the December 5, 2005 report that you reviewed to assist you in arriving at your

opinions in that letter?
A. We very rarely review other physicians' or other people's medical records when we diagnosis a patient in the environmental occupational neurology program. The reason for that is we --
Q. Did you have any in his case or not?
MR. GOTZ: Let me just ask that she be allowed to finish her answer before you ask the next question.
MR. MAHONEY: That's fine, but what I am -- I have said I am going to reserve on motions to strike, but many of the answers are not answers to questions. So let's try that again.
BY MR. MAHONEY:
Q. What medical records did you have of Coach Allen that you reviewed in arriving at this opinion, if any?
A. I don't recall what we had in our possession at the time. His wife probably brought some information with her. I think it is pretty clear everyone would know that she was still probably optimistic that we would not say it was ALS.
Q. So your answer is you don't recall?
A. I don't recall exactly what we had in our

possession.
Q. When you wrote this letter, did you make any reference to his previous treatment?
(Witness viewing exhibit 7.)
A. Yes, we did. We referred to Doctor Chad and Doctor Russell.
Q. Do you recall whether those references were based upon what he --
A. But I am not sure whether we had these in our possession when we saw him. We may have seen these after we saw him.
And I should state for the record that we do not look at other physicians' diagnoses when we make our diagnosis.
Q. Why not?
A. Because we don't want to be influenced by someone else's opinion. We try to go in de novo and arrive at our conclusion.
Q. Isn't it important to get as complete a history as you can from a patient before you arrive at your diagnosis?
A. It is before we make the ultimate diagnosis, but we like to see the patient -- and this is how I was trained, and Bob Feldman trained me this way from

his past experiences. We like to see the patient without any of those influences. We like to look at them and arrive at our own conclusion first because -- and many times, these cases do involve other physicians who may have been hired as experts or who knows what reasons they are involved in a case. We don't want their influences in our decision process at that point.
If we have seen the patient and we have made our conclusions, we then find supporting material that is in the history that we will refer to. We will refer to that. If there is history of things that exclude a toxic exposure, we will identify those things. If there is things that support a toxic exposure, we will identify those things and discuss them in context. But we very much just -- we just don't do that. And I think that is why we are held in the regard that we are, because a new broom sweeps clean.
Q. What documents did you review outside of these texts to assist you in arriving at the opinion that you have expressed in exhibit 2?
A. Exhibit 2 is which?
Q. Is your opinion.

A. Well, I have everything I have ever read in my life.
Q. No. Not -- let me -- maybe my question wasn't specific enough.
Did you review Mr. Allen's medical records to assist you in arriving at your opinion as expressed in exhibit 2?
A. Yes, I did.
Q. Did you review Mrs. Allen's deposition testimony to assist you in your opinion as expressed in exhibit 2?
A. I have seen that. I don't know if I used that in my opinion in any way.
Q. Did you review Mrs. Allen's answers to interrogatories in this case to assist you with your opinion as expressed in exhibit 2?
A. Again, you know, whether or not -- everything that is in here is based on history that was provided to me the day that I saw him. The history that was -- there was a list of materials that was like a diary that he wrote of his history to sort of get a perspective of some of the symptoms that he complained about, and my phone conversations with her, and, as I say, my interactions with him on the day that we saw him in clinic.

Q. When did you speak with Mrs. Allen?
A. I spoke with her the day that we saw him, obviously, in clinic, and I think I may have spoken to her on the phone prior to that.
And then there is probably times that I have looked at documents that she has or he has written to summarize the exposures, but other than their telling me that he complained of symptoms of such and such, that wouldn't influence my opinion in any way.
Q. Would you turn to page 7 of your opinion, please, under paragraph F.
A. Um-hmm.
Q. You see in the footnote there you say, "I have relied on the affidavits of one of the floor refinishers and several co-workers of Coach Allen, as well as Mr. Allen's written journals and the deposition of Ms. Allen."
A. Um-hmm.
Q. So it appears that you did rely upon those in arriving at this opinion. Is that fair to say?
A. As far as knowing the history of exposure, as I said, in the complaints, you know, the symptoms that he complained about, like I say, this journal that

he kept, reviewing that, and, you know, it is summaries of the complaints.
So this was a pretty -- his journal, his diary that he wrote was a pretty elaborate piece of material that reported his experiences.
Q. All right. When you wrote the letter to Attorney Agnelli of December 5, 2005, is it fair to say that you didn't have Mrs. Allen's deposition and you didn't have the affidavits as listed in footnote number one in page 7? Is that correct?
A. That's true. As I say, that is why.
Q. But you did have the journal that Mr. Allen had prepared, is that right, when you wrote the letter to Attorney Agnelli?
A. Again, I would have to go back to see what original materials we had in the folder at that time. But we did have a history from him that day in person and then whatever materials we were provided with that were in writing.
Q. Now the reference --
A. I take a history when the patient is there, and I write it down myself.
Q. Do you have those notes today?
A. No.

Q. Do you still have them?
A. I am not even sure if I do at this point. Sometimes those are just scribbles on my hands. Sometimes they are, you know, a page.
Q. What did you do to prepare yourself for today's deposition? What documents did you look at?
A. I reviewed my document. I reviewed the documents of the other witnesses in this case.
Q. On both sides?
A. On both sides, yes.
Q. Anything else?
A. You know, I am already pretty familiar with the material safety data sheets that were provided. And I reviewed the CIH documents from the industrial hygienist and others. There is a series of documents related to what chemicals were in the refinishing process.
Q. Did you review those in preparation for today's deposition?
A. (Witness nodding her head.)
Q. Okay. The references that you list in exhibit 3 which are listed on page 34-41 of your opinion, are these all texts and publications that you were familiar with at the time that you wrote the letter

to Mr. Agnelli, that is, December 5, 2005?
A. Were all of these? I don't know if all of these, but I would say a very large percentage of them I was familiar with. If you look specifically at other writings and other things, you can find references to these references or at least the same authors.
When I composed this reference list, I may have gone with a newer version for some. Barry Hallowell has a new paper. I have cited him before, but he wrote kind of an updated version. I use that reference.
Q. Let me ask the question another way.
The topics as listed in the references in page 34 through 41 is all subject matter that you were familiar with when you wrote the letter to Attorney Agnelli, is that right, December, 5 2005?
A. There may be one or two topics that I added to this document that bolster my opinion for the purposes of this affidavit.
Q. All right.
A. Those were documents that -- sometimes more recent publications than were available then. You know, in 1999 I with Bob Feldman wrote a paper saying that

polymorphisms and enzymes that metabolize drugs would be associated with a younger age of onset in neurodegenerative disease. The BU publication came out this year. So my understanding oftentimes benefits from time as the research gets done.

Q. But the -- I don't know how you express it medically or scientifically, but the bottom line of the subject matter, although research may have enhanced the opinions since you wrote the letter to Mr. Agnelli, you were familiar with all of the topics that are expressed in the reference list, page 34 through 41; is that fair to say?

A. When I wrote the letter to Mr. Agnelli, was I familiar with all the topics?

Q. Yes.

A. Actually, there are probably one or two topics that the general -- I would say --

Q. If you had to --

A. The general science, yes, but there are a few publications that have come out that just weren't there, so.

Q. If you had to assess a percentage of the subject matter that you were familiar with when you wrote the letter to Mr. Agnelli, what would that be?

A. 90 percent.

Q. So with that in mind, what I want to do is ask you a question about the opinion that you expressed to Mr. Agnelli on page 3.

Do you have that document in front of you?

(Witness viewing document.)

Q. By the way, this is an unsigned copy that was provided to me by plaintiff's counsel, but it is the same -- I just want to make sure that we agree. This copy here is on the letterhead of Boston University School of Medicine; is that right?

A. Um-hmm.

Q. And it has two signatures on last page which is Doctor Jabre's and yours; is that right?

A. Yes.

Q. Just so the record is clear, do you agree that the opinion, although it is on two different copies, is exactly the same? Do you want to take a minute to look at that?

A. Just let me look at it, yes, just to make sure. If there was a different version then -- there may have been.

Q. Here is the signed one, and here is the unsigned one.

(Handing documents to the witness.)

A. This looks like the same document, yes.

Q. So then I will have one in front of me and you will have one in front of you.

On page 3, you said, "The null hypothesis in this case states that exposure did not influence at age onset."

A. "Did not influence age at onset."

Q. "Age at onset." I am sorry. I have never been diagnosed with dyslexia.

What do you mean by that?

A. The null hypothesis is a phrase that is typically used in statistical research. But the null hypothesis states that there is no effect. The null hypothesis is there is nothing happening. So we reject the null hypothesis in statistical terms or epidemiological terms when something occurs. We have to reject the null hypothesis.

The failure to reject the null hypothesis when the data is consistent with rejecting it is what we call a type 2 or beta error in epidemiology. We have to be very careful not to make that mistake in a case such as this where there is not a lot of epidemiological literature.

So we have to -- epidemiology is a tool to support the observation seen in the clinical setting, and it is not within and of itself a stand-alone item. It is used to support an observation. But one of the fundamentals of that is the null hypothesis, and we either accept or reject the null hypothesis. If we accept the null hypothesis, that means that nothing happened.

In this case, he is exposed to chemicals. He gets ALS in chronologic relationship, and he gets it younger than would be expected. So it is very hard in this case to exclude or reject that the exposure had nothing to do with the onset of his symptoms simply because he got ALS, he got it younger than would be expected, and he was exposed to chemicals.

So we can no longer say that the exposure had nothing to do with his ALS because he was exposed to chemicals, and the chemicals he was exposed to are known to be neurotoxic, and he had symptoms of acute neurological dysfunction.

Q. Where do you draw the line in opining that the exposure did not cause ALS but hastened the development of ALS?

A. Where do you draw that line? I draw that line on the research that has been done to date. There is a tremendous body of literature looking at the incidence and prevalence of Parkinson's disease, the incidence and prevalence of ALS, and no one has ever found that any specific chemical causes any neurodegenerative disease.

And in my book chapter in the Parkinson's book, I specifically state that that is not surprising, because a toxic exposure, a toxic effect is just that. It is a toxic effect. And neurodegenerative disease is just that; it is a neurodegenerative disease.

And so simply by semantics, by simply language basics, you cannot say that the toxic effect is a disease. It is not. It is a toxic effect.

So since there is no literature supporting that, and it would be irrational to even state that a toxic effect was a disease, then --

Q. Or caused the disease?

A. Or caused the disease. Because if the disease were a toxic effect, it would be a toxic effect. It wouldn't be a disease any longer. And since the

interaction.

And oxidative stress is a huge problem. Depletion of glutathione is a huge problem. There is just -- it is just not a good mix for somebody.

Q. But have there been specific studies that have concluded that toluene hastens the progression of ALS?

A. Of ALS specifically, no. But there have been studies looking at motor neuron degeneration of toluene.

Q. We will get to those.

The opinion that you have that toluene hastened the progression of ALS, it is obviously based upon a sufficient exposure to toluene. Isn't that right?

A. Um-hmm.

Q. And in the studies that show that toluene causes neuron degeneration, how much toluene have those patients been exposed to to have the degeneration that you speak off?

A. That is not always known, because the -- after doing this for a long time, I can tell you people are exposed to chemicals occupationally. There is very infrequently accurate records kept.

epidemiological literature has never found any association with the incidence or prevalence of the disease, it is very reproducible. And not surprisingly so, since that would be a toxic effect and it would be very easy to do, it is pretty much not.

But as a modifying factor, toxic exposures are certainly relevant, and the whole train of logic in epidemiology and neurodegenerative disease is focusing more and more on the interaction between environment and disease progression today and less on incidence and prevalence. It is really steering away from that in recent years.

Q. What studies are you referring to that would suggest that exposure to toluene hastened ALS?

A. The studies I am referring to are the studies in my report that show how toluene can cause neurological dysfunction and that show how ALS causes cells to die and shows toluene mechanisms of action can interact with the mechanisms of action of ALS to hasten the progression of the disease.

It is simply a point of interaction, simply like two cars colliding. If they never hit, there is not an issue. If they hit, you have got an

What we do know from the history is they do often report symptoms, overt symptoms, dizziness and other symptoms, at some point during their career. Or if they are huffers, people who sniff toluene, they do that on purpose. They want to get inebriated.

Q. But that wasn't Mr. Allen's case?

A. No. He was not sniffing toluene.

But a case that we saw of the painter exposed to mix solvents who developed neurological problems reported in his history having worked in environments where he became dizzy from the fumes, and that would appear in my CV.

Q. You read the affidavit of Mr. Crecelius, didn't you?

A. I would have to look that over to remind myself. There is several documents.

Q. He was the floor refinisher.

(Handing exhibit 6 to the witness.)

(Witness viewing exhibit 6.)

A. I did see this, yes.

Q. In his affidavit, does Mr. Crecelius indicate how long he had been working for Martin Surfacing or Southwest Industries as a floor refinisher at the time of his work at the College of the Holy Cross?

(Witness viewing exhibit 6.)
A. He has been there for nine years.
Q. He worked there for nine years prior to this incident? In his affidavit, did he indicate whether or not he was using a respirator when he was working at Holy Cross?
(Witness viewing exhibit 6.)
A. "Protective gear is worn by the installers." "We use a full face organic filter respirator to filter out organic matters."
Q. Is toluene an organic matter?
A. Toluene is a volatile organic solvent.
Q. Are you aware of any complaints of Mr. Crecelius that he became dizzy or suffered any of the symptoms that Mr. Allen complained of following the floor refinishing process?
A. That is in his document there?
Q. Yes.
A. I would have to see it.
Q. Or from any source whatsoever?
A. Not to my knowledge.
Q. Given that he was a floor refinisher, wouldn't it be reasonable to infer that he had a more significant exposure to toluene than Mr. Allen?

A. Certainly a longer duration of exposure. But if he was wearing a respirator while he was on the premises, then his exposure would have been significantly reduced by the protective gear.
Q. What is the evidence that you are relying upon to support a quantitative amount of toluene that was in the air when Mr. Allen was allegedly exposed to these toxins from the floor refinishing process?
A. Well, there are studies that were done looking at symptoms --
Q. No, no. Let me rephrase the question.
What quantitative evidence in this case are you relying upon that show the level of toluene that he was exposed to when he was employed by Holy Cross?
A. I have no evidence on the specific quantity of toluene in the air. No measures were taken at the time. There were measures taken after the floor was done.
Q. Are those reliable in order to develop an opinion of the level of exposure that he was subject to at the time of floor refinishing process?
A. Say that again?
Q. The indoor air quality tests that were done at Holy

Cross subsequent to the refinishing process, do you have a memory of when they were done?
A. They were done in I think in two thousand -- it was after. It was maybe two years, then there was another one like -- one year, I think, and then two years after or several months after. And then there was a follow-up one that was done quite a bit later when the levels had subsided substantially.
Q. And you referred earlier to an OSHA standard?
A. Right.
Q. What is the OSHA standard for an acceptable level of toluene in an indoor environment?
A. 200 parts per million.
Q. In either of those studies, was there any evidence of toluene in the amount of 200 parts per million?
A. In what study?
Q. The indoor air tests. I'm sorry.
A. No. But those were done quite some time after, but the symptoms associated with exposure to toluene and the symptoms that he experienced are consistent with those exposures.
Q. What are the symptoms?
A. Dizziness, nausea. And these symptoms would be seen with mixed solvents as well. I use toluene in my

report as an example. It should be taken into consideration, because there were other chemicals there which would actually increase the toxicity of toluene by inhibiting its metabolism or possibly add to the toxicity of toluene but also sharing common mechanisms of action.
But nevertheless, he was exposed to concentrations of chemicals that were high enough to cause overt symptoms. And with regard to toluene, those symptoms would occur at concentrations above 200 parts per million. That is why the OSHA standard --
Q. How do you know that?
A. Because there are reports.
Q. How do you know they were high enough, and how do you know they were above 200 parts per million when he was exposed to them?
A. Because there are studies showing that exposures to toluene at concentrations of 200 parts per million and higher are associated with symptoms. Lower exposures are allowed to occur in the workplace because, obviously, they are not going to be associated with symptoms. You wouldn't want people walking around work all day dizzy, and, obviously,

if they are operating machinery, they would be a hazard to themselves.
Q. So correct me if I misstate your opinion. You are saying that because he had the symptoms, it is therefore reasonable to infer that he was exposed to toluene and other toxins at levels high enough to cause those symptoms?
A. High enough to cause those symptoms, or he would have been not experiencing symptoms.
Q. What efforts did you take to eliminate that he had been exposed to anything else that was causing these symptoms?
A. I, in here, do not exclude the other chemicals that were there. As I said, he was exposed to xylene. He was exposed to other chemicals. Those chemicals also can cause neurological symptoms. And the mix of volatile organic solvents collectively can cause an increase in neurological symptoms.
The toluene is known to be associated specifically with dizziness, headaches, and other symptoms at those concentrations. The isocyanates wouldn't cause those kinds of symptoms. So a lot of the other chemicals that were there would not cause that. The xylene, the methyl isobutyl ketone, could

cause similar symptoms, so those could have contributed to some of those acute symptoms.
Q. Is that your opinion, that they could have?
A. Well, their concentrations as a percentage -- and I would have to look back at the material safety data sheets -- would have to be taken into consideration and the percentage of toluene as far as what would have been the highest concentration of a volatile organic compound in the area at that time.
Q. Do the material safety data sheets with regard to the floor refinishing products in this case provide you with any information of the amount of toluene or any other toxin that emanates from the application of the floor when the refinishing process is ongoing?
MR. GOTZ: Objection.
Q. Do you understand my question?
(Pause.)
Q. Do you understand that? If not, I can rephrase.
A. Rephrase it.
Q. Do the material safety data sheets for toluene or any other toxin that was involved in this floor refinishing process provide you with a quantitative amount of those toxins that are emanated or

dispersed from the floor application process?
A. I would have to see -- well, the floor application process specifically? I would have to see the material safety data sheets. The amount of material in a material safety data sheet varies from manufacturer to manufacturer. Those are not always the same.
So I would have to go back and see the actual, specific material safety data sheet that was provided, because there is very -- the standards for material safety data sheets are not as consistent as we would like.
Q. Are you relying upon any information that was provided in the material safety data sheets that you reviewed related to the floor refinishing process to support your opinion that the levels of toluene and the other toxins in the area at the field house at Holy Cross were significant enough to cause the symptoms that Mr. Allen complained of?
A. Yes. There are material safety data sheets that show the percentage of toluene in the components of the resurfacing materials, and that is a document that I relied on.
Q. Was that attached to your opinion?

A. It is not attached to my opinion.
MR. MAHONEY: Let's go off the record.
(Recess taken at 11:21 a.m.)
(Recess ended at 11:40 a.m.)
BY MR. MAHONEY:
Q. Doctor Ratner, I am going to show you what are Bates numbers HC00031 through HC000074, which I will represent to you are material safety data sheets that we received from Dynamic Sports Construction, which is a company that, as I understand it, bought the assets of my client at auction, at a bankruptcy auction. And I want to know if these are the material safety data sheets that you relied on in forming your opinion.
(Handing documents to the witness.)
(Witness viewing documents.)
A. I have something different.
Q. It wasn't those?
A. They are not the same. There is a different set.
MR. MAHONEY: Let's go off the record.
(Discussion off the record.)
BY MR. MAHONEY:
Q. I think I need to clean up the record in terms of an exhibit that was previously marked. The opinion

that you provided to Attorney Agnelli I think we marked as exhibit 7, and it is my understanding that --

A. That was --

Q. -- this opinion was also supplemented by three pages of references, which is pages 4, 5, and 6; is that right?

A. Um-hmm.

Q. And those are the studies that you relied upon in co-authoring this opinion which we have marked as exhibit 7; is that fair to say?

A. Those are the studies I referenced. That doesn't mean those are all the studies I relied upon.

Q. All right. So just so the record is clear, exhibit 7 is actually six pages in length.

Now we talked about the reference to the OSHA standard of 200 parts -- it is per milliliter?

A. Per million.

Q. -- per million that are prohibited. Amounts above 200 parts per million are prohibited by OSHA; is that right?

A. That is a time-weighted average, so the time-weighted average over the course of an eight-hour period should be 200 parts per million.

It can exceed that, but then is has to be below that, so.

Q. So the average in any eight-hour period cannot be more than 200 parts per million?

A. Yes.

Q. And do you have an understanding of the basis for that?

A. That is based on a review of the scientific literature which includes animal studies, human studies, which is effectively relied upon by OSHA to establish an exposure limit.

So OSHA reviews the literature and then ascertains from that what they feel is a limit that should be not be exceeded.

Q. And is that limit that OSHA has set for an eight-hour period based upon a study that is referenced --

MR. MAHONEY: Strike that.

Q. What is your basis for understanding what OSHA relied upon in order to set that limit?

A. That limit is the current limit. There was actually a lower limit of 100 parts per million that was kicked back because OSHA had used NIOSH to come up to that conclusion, and so those were --

Q. Had used what?

A. NIOSH. National Institute of Occupational Safety and Health.

Q. Okay.

A. And it was concluded -- there was a lawsuit of some sort or something -- so they rolled back to the old standard of 200 parts per million.

There is a considerable amount of literature out there to support that it should be 100 parts per million, but OSHA has to go back through the whole process again to get it back to that level. In other countries, I think it already is 100 parts per million.

Q. Okay. But what I am asking about is the research that OSHA bases its standards upon. It is research of what nature?

A. It is research from all aspects. They look at the animal research, they look at the epidemiology research, and they look at the mechanism of toxicity research, the in vitro study, and they collectively use their information to ascertain an exposure limit that should be safe.

And those limits are then enforced until new research comes out that may make that be higher or

lower.

Q. Is any of that research inclusive of a study that suggests that exposure to toluene of the 200 parts per million will hasten either the onset or progression of ALS?

A. Well, I will read to you what OSHA states on their website from my report, and I will let you be the judge of that.

(Witness viewing document.)

Q. There is a reference to it on page 19, paragraph 5. I don't know if that is what you are looking for.

(Witness viewing document.)

A. No. There is another statement that they make.

(Witness viewing document.)

MR. MAHONEY: Let's go off the record for one second.

(Discussion off the record.)

MR. MAHONEY: On the record.

THE WITNESS: "According to OSHA, 'before a worker is placed in a job with a potential for exposure to toluene, a licensed health care professional should evaluate and document the worker's baseline health status with thorough medical, environmental, and occupational histories,

a physical examination, and psychologic and laboratory tests appropriate for the anticipated occupational risks. These should concentrate on the function and integrity of the central nervous system and skin. A preplacement medical evaluation is recommended to assess an individual's sustainability for employment at a specific job and to detect and assess medical conditions that may be aggravated or may result in increased risk when a worker is exposed to toluene at or below the prescribed exposure limit. The health care professional should consider the probable frequency, intensity, and duration of exposure as well as the nature and degree of any applicable medical condition. Such conditions (which should not be regarded as absolute contraindications to job placement) include a history and other findings consistent with diseases of the central nervous system and skin."

BY MR. MAHONEY:

Q. Can you tell me what paragraph and page you were reading from?

A. Page 29, section K, paragraph 2.

Q. You started by reading paragraph 2?

A. Um-hmm.

Q. And when did you stop?

A. At the end of paragraph 2 on page 30.

Q. I think I asked if the OSHA studies specifically relied upon a study that suggested that an exposure to toluene above 200 parts per million hastened the progression and the onset of ALS.

A. Um-hmm.

Q. And you read from page 29 and 30 of your opinion a warning from OSHA for employers about precautions to take when they were exposing an employee to toluene; is that right?

A. Um-hmm.

Q. So is there a study or is there not a study that you are aware of that specifically says that exposure to toluene of 200 parts per million will either hasten the onset or hasten progression of ALS?

A. No, but may I qualify that?

Q. No. You have answered the question.

Is there a study that says that an exposure to toluene of 200 parts per million, an animal study, will hasten the onset or the progression of ALS?

A. No.

Q. But that is your opinion as we have documented today in the deposition, that Mr. Allen was exposed to a toxic substance, likely toluene, in an excess of 200 parts per million, which hastened the onset or the progression of ALS; is that right?

A. That is correct.

Q. Have you ever provided an opinion such as you have expressed today with regard to any other human being other than Mr. Allen?

A. With regard to ALS and its progression in relation to toluene?

Q. Yes.

A. No.

Q. Now you indicated at the start of the deposition that the primary focus of your vocation is research; is that right?

A. Um-hmm.

Q. So would it be fair to say that you have been involved in a number of research, clinical research projects, clinical studies?

A. In various capacities. I was the project manager of the gene environment metals interactions Parkinson's study, which was a collaborative study between Harvard and Boston University.

Q. And many others?

A. That was during my training in the department of neurology. Since then, I have elected to do in vivo animal studies, so I have gone away from human clinical research, based largely due to my interests in increasing my ability to do the type of research I am interested in.

Q. But in any event, the focus on your life's work -- I don't mean that to sound as lengthy, because I know you are a young person -- but the focus of your employment has been participation and from a scientific research point of point of view of a number of studies, whether they were animal studies or human studies; is that right?

A. Um-hmm.

Q. So are you familiar with, generally speaking --

MR. MAHONEY: Strike that.

Q. Are there any --

MR. MAHONEY: Strike that as well.

Q. Any of those studies that you have participated in, have they ever been published?

A. There is one. My own research in Parkinson's age of onset is in preparation, and that will be published.

Q. Can you explain to me the process? Let's just focus on that one. You anticipate that that will be

published, what, in the near future?
A. Um-hmm.
Q. Can you explain to me as a lay person the process of evaluation that is involved in the decision to publish the type of study that you anticipate will be published?
A. So, someone will -- you will submit a paper for publication. It will be reviewed by other persons with expertise in the area for methodological and scientific value. So you will look to see does it contribute something new to the science or meaningful to the science and then are the methods employed the proper methods.
Q. Reliable?
A. The proper methods, right.
Q. Anything else that is involved in the evaluation to determine whether or not the study will be published?
A. That is the two main criteria. That is, the scientific value. Does it contribute something meaningful?

And the third thing is, sometimes, the editor. What does the editor want to see in the journal that you have submitted to? So the editor

may not be interested in that topic right now, so you have to submit it to a different journal.
Q. But that is more of subjective?
A. That is the third criteria.
Q. I am talking about objective criteria. The study, before it is published, is examined for its methodological reliability and its scientific value; is that fair to say?
A. Yes.
Q. And as a part of an evaluation of the methodology, is there any protocol or criteria that is employed that suggests that a certain number of subjects, be they animal or human, must be used to validate the findings?
A. Yes.

MR. GOTZ: Objection. You can go.

A. Yes. You look at something called statistical power is one thing that you will use. In the case of a single case study, that criteria does not apply. If you are doing an epidemiological study, the magnitude of the effect -- for example, if I have a very, very strong high dose of a drug, I could see an effect in an N of 2.

My colleague, Conan Kornetsky, often likes

to say, "If I told you that I had a dog that talked and I brought that dog in here and it spoke, would I need more than an N of 1 to justify my point?"

The N is only important when it comes to the magnitude of the responce. Generally, we like to have at least an N of 8 if we expect a 50 percent difference in responding with 25 percent variance. That would allow us to have enough power to measure that effect. An N smaller than that, you would have to have an even greater change in responding with a limited amount of variance. With greater variance and a smaller effect, you need to have a larger N.

So the sample size is related to the question at hand, what you are looking at, how powerful is that effect. If it is a very subtle effect, you need to have a larger N. If it is a very strong effect, you can have a small N. So that is what is called statistical power, what is the power of the study.
Q. So is it your position, then, that the effect that you studied with regard to Mr. Allen and the toluene's effect on hastening the progression of ALS is such a powerful effect that you don't need a large sample size to justify the reliability of your

opinion?
A. In Mr. Allen's case, we have -- when I said we reject the null hypothesis, we have an exposure that we know occurred and we have an outcome that we know occurred. So we cannot any longer exclude the role of the exposure since we know he was exposed to a neurotoxicant, several neurotoxicants, through the course of him being in that location. And so our question then becomes not one of an effect, but becomes one of the magnitude of the effect. How robust is that effect.

If you look at the bell curve, we have -- what we decide on is the middle of that bell curve. We say, "This is the median, the mean change in effect."

But on both ends of the bell curve, we have people who get sick sooner and people who very rarely get sick. The most susceptible individuals, those with latent neurological disease, those with polymorphisms in genes that inhibit metabolism of compounds, they get affected at much lower doses. Those with polymorphisms that enhance metabolisms and no latent disease can withstand much more of a hit before they have a problem.

That gets at your question of why this man who worked for so long didn't have symptoms of any problems that affected his livelihood while Mr. Allen did. That man, to the best of our knowledge at this point, is not walking around with a latent neurological disease that could have been unmasked. Maybe he will someday reveal that that is true, but at this point we don't know that he does. It is just simply a matter of susceptibility and how hard and how many hits an individual can tolerate.

Q. And I would like you to just answer this as yes or a no. So it is your opinion that the reliability of your opinion in this case is justified even though this is a single case study because of the magnitude of the response that Mr. Allen allegedly endured during exposure?

A. Because of the -- you want a yes-or-no answer?

Q. Yes. Is that your opinion, that even though you don't have an N of 8 or N of 100, you have an N of 1, that that is all you need to justify your opinion in this case?

A. In this case, yes. With a caveat that the scientific mechanisms of action and other factors are considered in that opinion. It is not just,

"Well, he got sick, and that is my opinion." It is all encompassing.

Q. And when you talk about the scientific mechanisms of action, you are talking about what you alluded to earlier, about the known fact that toluene causes neurodegeneration and the known fact that ALS causes neurodegeneration; is that right, generally speaking?

A. That's correct, generally speaking.

Q. But if you wanted this opinion in this case, in Mr. Allen's case, to be published, it would have to be subjected to peer review, wouldn't it?

A. Yes.

Q. And has this opinion been peer reviewed?

A. It has not. At this point, it has not been submitted for publication anywhere.

Q. What is your intention in that regard, if any?

A. Well --

Q. You are the author. Do you have any intention to submit it for peer review?

A. Yes, actually. I was planning on presenting it at Grands Rounds at Harvard in the fall.

Q. At where?

A. Harvard School of Public Health.

Q. And then it would be subject to peer review?

A. And then I would probably publish it.

Q. Assuming it was accepted?

A. Um-hmm.

Q. And if it was rejected, how would that affect your opinion?

A. It wouldn't change my opinion.

Q. But at that point, it would have been rejected by peer review and deemed not worthy for publication?

MR. GOTZ: Objection. You can answer.

A. Yes. It would depend. Oftentimes, you have to submit the article to multiple journals. As I said, the editor may not be interested in this one case. Another journal may say it is great.

Usually, you have to submit them more than once because it comes back, "Well, we like it, but we would like to see some changes."

So the submission process is not an all-or-one or all-or-none process. You go through finding a journal that is appropriate. Sometimes you think it is appropriate, but the editor doesn't. And so, you know, the peer review process is fairly complex, so it wouldn't necessarily mean that, because we don't know why the editor decides not to

accept it. If critiques came back and said, "This is wild madness" or something, but I don't think that would be likely considering that I have had related materials published.

Q. What step in the process is the seminar that you expect to present it at? That is just, what, an airing of your opinion?

A. That is just presenting it, airing the opinion in an environment of peers where they can ask you questions and think about things. This is pushing the envelope of medicine, so Grand Rounds is a place where physicians come to think about novel ideas, what is pushing the envelope, where are we going with research.

This would be presented in context with other research in neurodegenerative disease that has been coming out showing how environment and neurodegenerative disease are interacting in an age of onset fashion less than they are in an incidence and prevalence fashion.

Q. So you would present it at this, what, this is a consortium?

A. Grands Rounds is where occupational health physicians at Harvard come to weekly. Usually you

come to Grand Rounds and you hear a speaker talk about a topic, whatever that topic may be, and its relationship to occupational medicine.

Q. Are you scheduled to present this paper?

A. The date hasn't been chosen. It has been submitted and proposed as a topic for the fall. I had proposed it for the spring, but actually it didn't get slated because the schedule was already --

Q. Who did do you propose it to?

A. Stephen Kales.

Q. And he is at Harvard?

A. Yes.

Q. What is his title over there?

A. I think he is the director of the occupational health program.

Q. And then he decides whether or not --

A. He decides what topics are appropriate and what should be included this semester. Again, it is like an editor, depending on, you know, what the focus is.

Q. But that is not a peer review, per se, is it, when you present it like that?

A. Well, in some ways, it is because the audience is all your peers who have the opportunity to ask you

questions at that point and criticize your work, or --

Q. On the other hand, if Kales did not schedule you to present it, there is another process of peer review that you could go about; is that right?

A. Well, I could submit it for publication elsewhere.

Q. So is it your -- let's assume that Kales says, "No. I don't think this is appropriate." Do you still intend to submit it for publication elsewhere?

A. Yes. More likely than not.

Q. To what type of journals?

A. You know, probably journals in occupational medicine or neurology. I might submit to it to the Journal of Neurology. I might submit it to Muscle and Nerve. I might submit it to the Annals of Neurology, Archives of Neurology. I might submit it to some lower journals. Those are the highest ones that I would consider. I might also look at some occupational medicine journals like --

Q. But today, as we sit here, you would agree that it hasn't been subject to peer review?

A. Not at this time.

Q. What I wanted to ask you about earlier was if there are any recommendations made by physicians who

diagnose ALS to their patients about certain things that they should avoid because it will exacerbate their condition and make their quality of life less than it is.

A. I know when I would be in clinic with Bob Feldman, we would advise patients with Parkinson's or ALS to avoid chemical exposure to not hasten the course. Conversely, we would be looking to, in treating them, to prescribe medications like Riluzole that could slow the progression. So you want to do anything you can to prevent the progression. You want to do everything you can ti extend the quality of life. So it is obviously a both thing.

Q. What is the -- I am going to ask you to educate me.

What is the medical term that I am looking for? Not diagnosis, but once the diagnosis has occurred -- recommendations, I assume.

Are there any recommendations, published recommendations that you are familiar with that you specifically tell a patient who has been diagnosed with ALS to avoid toluene?

A. There is nothing that I know of specifically stating that, but if I can qualify that, I think OSHA's statement right here that people with neurological

problems avoid exposure to toluene. That is about as close as it can come.

Q. But that is an OSHA recommendation rather than a medical recommendation; is that right?

A. That's correct.

Q. Would you agree with me that toluene is ubiquitous, found in common household cleaners, et cetera?

A. Yes.

Q. What steps did you take to eliminate the probability that Mr. Allen had been exposed to toluene in other environments other than what you suspect occurred at Holy Cross?

A. We saw him. We asked him his history. We knew he worked as a football coach, so we wanted to know his occupational history, what he did for a living. We take that into consideration. Hobbies. We looked for other sources of exposure.

In Mr. Allen's case, he wasn't painting cars in his garage and he didn't work in an industry where he would be exposed to toluene. So there was no reason to believe that he would have been exposed to levels higher than background levels that occur in environmental exposures for most people, which would be relatively low levels.

And so there was nothing in his history to suggest that he was being para occupationally exposed or environmentally exposed. There was no problem with his family as far as reported symptoms that could be related to drinking water or anything like that, so.

Q. Is there any -- I meant to ask you this before we broke. Is there any medical test, for example, a blood test or a tox screen that would document and quantify any --

MR. MAHONEY: Strike that.

Q. Once you have an exposure to toluene, how does it manifest itself in your body? Can you test the blood for it? Or can you do a toxicology screen?

A. You could measure concentrations in various places. You could look at end exhaled air. You could look at the concentrations of metabolites, the parent molecule in urine and blood. Just, you know, there is various ways you could detect it. Remote exposure with volatile organic solvents. Because, unlike heavy metals, they don't bioaccumulate in your hair as well. So generally, you have a limited window of time that you can measure it.

Q. Do you have to specifically test for toluene, or

would it be included in a regular blood test or a regular toxicology screen?

A. It would never be done ordinarily.

Q. So you would have to be specifically looking for it?

A. You would have to be looking for it. They don't -- I can't think of any circumstance where you would randomly screen.

Q. When Mr. Allen was seen at UMass. Medical Center by Doctor Chad, do you recall whether or not there were any blood tests or toxicology screens done of him at that time?

A. Off the top of my head, I don't know what tests were done. I would have to go back to the record to see.

MR. MAHONEY: Let's get those. Just get them all.

A. I would say it is fair to say that the duration of time when he saw him and monitored his blood levels would be sufficiently far away from the exposure to not measure measurable levels, even if it were done. The half life of toluene is not long enough to detect high concentrations that could be associated with neurological disease that far out.

Q. Then educate me on how it continues to hasten the effect of ALS. If you can't measure it in the body,

what happens? He gets an exposure to it, and then the concentration of it leaves the body, but the damage has been done and continues to occur? Is that fair to say?

A. Yes. Because there is actually changes in the body that -- I think I pointed out before -- for example, oxidative burden is increased. Glutamatergic neurotransmission can be altered. And what happens is that even though the toluene is gone, its influence on the cascade remains.

And the hit -- so if we think of it as a car accident, the hit occurs; the damage is done; the cars drive away. The car with the damage still has the damage, and then that damage may start to rust and other problems may start to occur that add collectively to exacerbate that.

But the major impact of the exposure and its influence of the disease occurs within a very short period, a very short window. There is some ongoing continued progression, but the major impact on the progression is during that window. And then gradually, with time, its influence trickles down to be minimal. But by that point, the damage is done. The impact, the shove that has been given, is

already in place even though the ongoing toxicity has ceased.

Q. Can ALS be caused by trauma?

A. I think that there are some research that has made some associations between trauma, but I don't know that we can say that it is the cause of ALS any more that we can say that anything else is the cause of ALS. I think that trauma, like a toxic exposure, can exacerbate ALS. The same thing, the loss of neurons associated with the trauma can additively interact with the loss of neurons associated with the neurodegenerative disease process.

So maybe you see a slight increase in the incidence, maybe because people who would have died from something else developed clinically overt symptoms before they died from something else, and they get added into the pile of people that are diagnosed with ALS.

So this is where the epidemiology looking at incidence and prevalence is somewhat confounded by this interaction of environment and environmental factors with the disease. It happens with blunt trauma. It happens with so many factors.

If you look at Parkinson's disease on head

injury incidences, you see the same kind of thing.
Q. And what is the half life of toluene that you referred to earlier?
A. I don't recall it off the top of my head.
Q. Is there anything that you have with you today that would assist you in determining that?
A. No. I don't know. It is not that long. Basically, for most volatile organic solvents, it is not that long. These compounds come in and out of the body within days. In pretty much hours to days, they are gone. They are metabolized very quickly, and then they are excreted. They don't stick around the way heavy metals, for example, like lead. Lead can bioaccumulate in your body for 25 years and still be present. It is stored in bone.

But with the volatile organic solvents, they are gone within hours to days. It is pretty fast. And it depends where you are measuring it. It stays in higher concentrations in the fat and may persist longer than concentrations in the parenchymal organs. In blood --
Q. You are talking about lead?
A. No. I am talking about toluene in this case.

It could bioaccumulate for a longer time in

fat because it is lipophilic, so it may hang around in fat longer than it would in the blood, for example. So if you did a fat biopsy, you might be able to document an exposure further away from the actual incident than you could by measuring blood levels because the lipophilicity of the compound would allow it to stay in the fat longer. And the fact that fat is not well perfused, it wouldn't be carried away very quickly. It would stay there longer. But that would be a very invasive study, and it normally wouldn't be used in biological marking.
Q. What are the recognizable effects of the exposure to toluene, for example, within the first two to three months following the exposure? Dizziness, I think you said?
A. These are acute symptoms that generally resolve with the cessation of exposure. Damage to neurons, once it is triggered, can take days or weeks to manifest.
Q. But what are the acute symptoms? Nausea and vomiting?
A. They resolve, generally, within hours to days.
Q. And if they persist?
A. If they persisted longer than that, that would be

unusual unless the exposure were high enough to have such long half life that it would persist longer. But you would be unconscious, probably, if it lasted more than hours to days. You would have to have such a high body burden, and you would probably die at that point.

So generally, the symptoms resolve spontaneously within hours to days. There wouldn't be, normally, a situation where they would persist beyond that.
Q. Would you expect to see elevated liver functions if he had been exposed to toluene?
A. It depends. If you are looking at abnormal liver functions, some solvents -- like you might see an abnormal liver function, what we would call the critical effect. But in the case of toluene, the change in liver function may be very subtle and unmeasurable.

Generally you would see with toluene maybe an induction of liver enzyme activity, but you normally wouldn't be measuring that. You would be looking at ALT, other bilirubin, alk phos. You would be looking at things that you wouldn't look for to look for changes in liver function associated

with toluene in the normal medical assay. It is just not done.
Q. What effect would toluene have on bilirubin?
A. You wouldn't expect to see anything, really, and generally, in general, the effects would probably be -- unless a person were exposed for a very long time where they started to develop cirrhosis of the liver or something to this effect which would cause an increase in bilirubin. Or if you -- something like this, but I mean generally that wouldn't be a biological marker that you would use to measure the effects of toluene on liver function. If you were doing studies, you would be looking for other factors.

If the exposure were high enough and long enough, you might see changes in ALT, AST, other markers of liver function, but the liver is much more resilient than is the nervous system. So those changes would again probably resolve with the type of exposure that Mr. Allen experienced.
Q. When you and Doctor Jabre examined Mr. Allen in December of 2005 -- no. I'm sorry. It was April of 2004. You examined him in April of 2004. This report is dated December of 2005; is that right?

A. That is correct, yes.
Q. Why didn't you prepare a report immediately following your examination of him in April of 2004?
A. There is two ways that report is prepared. There is your working note that goes into, perhaps, a file where you just say "saw him, did this examination," and there is several documents that would have been -- that is what we call a clinical note that just documents what you saw.

The report is something that was asked for later, and this is not normally a report that you would put in a patient's file. This report was asked for by Joseph Agnelli. When we saw Mr. Allen, it was for the purpose of establishing a causal relationship between, first of all, does he have ALS. That was the first question that we wanted to ascertain. And then could the exposure contribute to the ALS was the second question that was asked.

For our purposes, we could have just seen him and left it at that and never given a report unless someone asked for one.
Q. So I think you said it was Attorney Alan Bell who contacted --
A. First contact with us was Attorney Alan Bell, who --

Q. Did you prepare a document for him?
A. I don't believe so.
Q. Do you have a file regarding Mr. Allen that you maintain at your clinic?
A. Much of my stuff is kept, actually, on my computer, and so I have electronic copies. Like there is an electronic copy of that letter kept on my computer. I mean I have materials related to this case, but most materials just, you know, I just put it in my computer. I don't want to have paper anymore.
Q. Did you rely upon any notes that you had taken during your examination of April 2004 to assist you in drafting the opinion to Mr. Agnelli?
A. As I say, I may have had some scratch notes of just observations. And then I would have looked -- in addition, this incorporates -- Joe's clinical notes were incorporated in there as far as the deep tendon reflexes and other aspects of his examination. And so, you know, the two of them would have been then combined, my scientific understanding of the interactions and Joe's observations of the examination.
Q. What type of an examination did Doctor Jabre do on Mr. Allen in April of 2004? In order words, did you

witness it?
A. Yes.
Q. So what did he do?
A. I would call it an a general neurological examination. He looked at DTRs. He looked for sensory and motor function. He looked at the bulbar signs. He, you know, in addition to taking a history and what we would call just your veteranary neuro exam, basically standard neuro exam.
Q. Was he given a neuropsychological examination?
A. Not at that time. If that was done, it would have been done on a separate occasion. But to the best of my knowledge, that was never done by us.
Q. At your clinic, is that the type of thing that can be done?
A. We do, yes. We do, but it wasn't done.
Q. Who usually gives that examination?
A. Those examinations are done by Roberta White and some of the people who work with her, Maxine Crangel.
Q. And why was Mr. Allen determined not to be a candidate for a neuropsychological examination?
A. At that time, there was no complaints of cognitive problem areas that were being pursued. I think we

came in and saw him with a question of the motor neuron disease and to confirm the diagnosis of ALS initially. There was some question at that time. I think his wife was reluctant, as I said, to accept the diagnosis, and to some extent I think he was hoping we would tell her it wasn't ALS.

And so I think part of the reason that that may have, you know, there was communications to her saying, "Look, sorry to tell you this, but your husband has ALS." She didn't want to accept it, I don't think, up until the end.
Q. Is there any study that identifies any cognitive deficits that can be caused by an exposure to toluene?
A. Yes.
Q. Is that a common result, cognitive deficits?
A. Yes.
Q. Yet there was no report of him having any cognitive deficits in this case; is that right?
A. Whether or not he had them, they may have taken a back seat.
Q. I am asking you if anyone ever reported to you or to Doctor Jabre that he had any cogitative deficits.
A. I don't recall them being considered a problem for

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him. He wasn't complaining of them at the time. It didn't mean he didn't have them, but obviously he had a lot of other problems that were probably more important to him.

Q. But given that toluene can cause cognitive deficits, if a neuropsych exam had been performed and it was determined that he did have cognitive deficits, that would bolster your opinion that he had been exposed to toluene, wouldn't it?

A. Absolutely.

Q. But we don't have any evidence of that, do we?

A. No. Like I say, he died shortly after we saw him. So even if we had wanted to run those tests, which, you know, if -- as I say, when he first came to us, we were really just making a diagnosis. I think, you know, we probably would have pursued that, but it just didn't happen to a large extent, possibly, because he died. So there was not time. There was no opportunity to pursue that.

I, generally, in a situation like this, do like to order a neuropsych assessment, because having both aspects does bolster the position, but in this case -- and as I said, given his problems, even if he was having memory problems, I don't

think -- or attention problems --

Q. Was he able to communicate with you when you saw him in April?

A. It was very difficult for him to communicate by that point.

Q. Could he have endured a neuropsych examination at that point?

A. I don't think he would have endured one, anyway. So if he did, it would have been very, very difficult. So that is another reason, again, why we just wouldn't have ordered one. The whole circumstances at that point were pretty sad.

Q. Do you disagree with the immediate cause of death as recorded on the death certificate of neuromuscular degeneration?

A. I think that is a broad statement that includes ALS.

Q. So you agree with that?

A. Yes.

MR. MAHONEY: Why don't we stop here.

(Luncheon recess taken at 12:34 p.m.)

AFTERNOON SESSION

1:33 p.m.

BY MR. MAHONEY:

Q. Doctor Ratner, can you define for me the realm of direct empirical support for your opinion? Outside of your opinion, are there any other studies that support your opinion that toluene hastens the onset or progression of ALS?

A. Specifically toluene, no, but I should qualify that if you like.

Q. What is your qualification?

A. There are studies that have looked at, in animal models, the interactions between chemicals and ALS, and toluene is a chemical. And they have looked at the interaction as far as slowing the progression and hastening the progression of the disease. So in that regard, this topic is being studied extensively, primarily in the pursuit of pharmaceuticals to slow the progression. Obviously, you wouldn't want to have something to hasten the progression.

Q. Are there any specific animal studies that focus on the effects of toluene on hastening ALS?

A. No.

Q. How do you involve ALS in any animal study? I mean how do you find mice with ALS?

A. You make them. You make a transgenic animal with a superoxide dismutation that is more susceptible to motor neuron degeneration, and then you apply chemicals to that animal, and you try to modify the clinical course of the disease one way or the other.

Q. So you breed mice that have a motor neuron -- susceptibility to motor neuron diseases?

A. Um-hmm.

Q. But as yet, there are no studies that link toluene to hastening the onset or progression of ALS, no animal studies or human studies?

A. Those have not been done, to the best of my knowledge.

Q. What about studies that suggest that toluene may hasten either the onset or progression of Parkinson's? Are you aware of any such studies?

A. Specifically? Not specifically toluene, per se.

Q. But just other chemicals?

A. But other chemicals have been studied.

Q. Just so we can focus your opinion a bit more, it is your opinion that the toluene that may have been in the floor refinishing products is the major

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predominant chemical that adversely affected Lou Gehrig's disease in Mr. Allen?
A. Again, I would say yes, but I would qualify that.
Q. How would you qualify it?
A. I would say that the other chemicals that were there play a role as well.
Q. What role?
A. For example, as I cite in my work here, other compounds will compete metabolically with toluene. They may require glutathione conjugation for elimination, which would further deplete glutathione stores.
These interactions -- and as I state in that report, I used toluene as the example because there was a high concentration in the mixture of the chemicals involved and because it is well studied. But the other chemicals that were there could have interacted with toluene to increase its toxicity, and there may be the possibility that some of the metabolites of the compounds that have not been fully elucidated could have their own toxic profile. I have to rely on science as it exists. I can't speculate on mechanisms that there is nothing known about.

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So from what is available, toluene is the compound that I use as my example, but I would not say that the other chemicals had no contributing factor. I think they may have played a role as well.
Q. Is that as close as you can get to any level of scientific certainty that they may have contributed a role?
A. Again, the toxicity of xylene is -- I will say yes. Can I qualify that?
Q. Sure.
A. The toxicity of xylene is known to be considerably lower than toluene. In fact, it is a substitute oftentimes for toluene when possible as a solvent because of that. But it doesn't mean that its presence in the body could not contribute in some ways to the progression.
Stoddard solvent, too, is relatively lower in toxicity than toluene, but if there is competition metabolically, then toluene metabolase levels in the blood would be altered in ways that may contribute further to its toxicity.
Toluene is, of the solvents that were present, more toxic in general than xylene, for

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example, and the concentrations of it was -- it was a significant component of the materials that were used in the surfacing process.
Did we ever get that material safety data sheet, by the way?
Q. Yes, I think we have it. I will get to that in a second.
So you correct me if I misstate your opinion. It is your opinion that the toluene that is alleged to have existed in the floor refinishing products hastened the onset and/or progression of ALS in Mr. Allen, and that is your opinion with a reasonable degree of scientific certainty; is that right?
A. Yes.
Q. But it is not your opinion with a reasonable degree of scientific certainty that the other chemicals that may have been present in the floor refinishing products hastened the onset or progression of ALS; is that right?
A. I -- no. That is not a correct statement.
Q. Can you say that other chemicals other than toluene hastened the onset or progression of ALS with a reasonable degree of scientific certainty?

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A. Not with as reasonable a degree as in the case of toluene. Certainly, they do not, based on their mechanisms of toxicity, based on their -- I would not be able to say that they played as important a role, but I would not say that they played no role. I think that their role is ancillary more than is toluene. So they would interact with a disease but not as substantially based on what is known about their toxic profile and their mechanisms of action.
Q. Were you aware that in 1996 Mr. Allen had complained of hypertension for 10 years and a had family history of hypertension?
A. The medical history shows that there is a family history, and he had hypertension when he was seen.
Q. Is that of any significance to you in regard to the later diagnosis of ALS?
A. You take the patient as you find him. Every patient comes with a history. Everything in his life that he experienced prior to the onset of his symptoms and since the onset of his symptoms in some way contributed one way or the other to the progression of this disease.
As I already stated, if he took multivitamins, maybe that slowed the progression.

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If he had taken Riluzole, maybe that slowed the progression. If he had exposure to other chemicals, if he had worked with chemicals in another job capacity, that could have hastened the progression. So we have to take the patient as we find them, and all of that is taken into consideration in my opinion.

Q. So it is your opinion that a condition of hypertension contributed to the final diagnosis of ALS?

A. As I said, we take the patient as we find them. The hypertension, if it was not controlled and led to small strokes and neuronal loss, that could be a problem. I don't know that there was an indication of him having uncontrolled hypertension that was causing him small strokes. So I, at this point, you know, would say that the contribution would not be as remarkable as the toluene since there was no evidence that he was having neurological problems related to the hypertension.

Q. Would a small stroke be evidenced through a CT scan?

A. Oftentimes, you can seen small strokes on a CT scan as little -- small parenchyma, just little areas of -- they sometimes show up.

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Q. Were you aware that in 1996 he also complained of a neural headache two or three times a week, frontal constant, and that it occurred during the day, no changes in the week, and it had been ongoing for about three to four years?

A. Yes. He seemed to have persistent headaches in his history. You know, headaches can be vascular in origin. They can be tension. It is -- you know, changes in his life, changes in jobs, other things that may have influenced him could cause stress and headaches. So I don't know that that in and of itself is of any relevance.

Q. All right. So in your opinion, the evidence of neural headaches is insignificant in terms of the ultimate diagnosis of ALS?

A. I would say you take the patient as you find them. Their whole life is -- you don't say that something has no merit. There is no, again, no indication that those headaches were due to a stroke or anything like that. So, you know, I don't know for sure the cause of those headaches, and they don't seem have to have had any sequelae beyond that of a headache.

Q. Are you aware of any study that links doses of

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cortisone to an ultimate diagnosis of ALS?

A. Again, you know, there is probably, you know -- I am not aware of one in particular that would say high dozes of cortisone would cause ALS. I don't think that would be reasonable to assume.

Q. Are there any negative effects of cortisone injections that you are aware of?

A. Again, every drug is associated with risks and benefits. And again, you have to take the patient as you find them. So any drugs that he was using would not be without consequence one way or the other.

Steroids can act on the nervous system. I do research on steroids and their relations to neurological function. They can enhance glutamatergic neurotransmission; they can inhibit glutamatergic neurotransmission. So, you know, the interaction of any compound with the disease is something that has to be taken into consideration.

Q. Are you aware of Mr. Allen having taken any steroids during the course of his life?

A. From the top of my head, I would have to look back at his medical records to see exactly what he was taking. But if my memory serves me right, that was

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in there and one of the things he may have taken. He was an active individual.

Can I see access to --

Q. Which documents are you referring to?

A. His medical records.

Q. Which one specifically?

A. Let's see. I would have to see all of them a5 this stage of the game just to confirm exactly what he has been on.

MR. MAHONEY: Let's go off the record.

(Discussion off the record.)

MR. MAHONEY: Back on.

BY MR. MAHONEY:

Q. Let me show you, Doctor Ratner, the medical records that were provided by Doctor Polkin's office, which I understand to have been Mr. Allen's primary care doctor. I ask that you look at those and see if you see any records of steroid use.

(Handing documents to the witness.)

(Witness viewing documents.)

Q. Let me ask you a general question if you don't mind while you are looking at that.

A. Sure.

Q. When you were referencing steroid use, were you

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thinking about cortisone or other types of steroids?
A. Steroids in general.
Q. And cortisone is a steroid; is that right?
A. Yes.
(Witness viewing documents.)
A. These records don't go back far enough.
(Witness continuing to view documents.)
A. These records wouldn't go back far enough or be complete enough to see if he had a history of use of them. I don't know. Again, my response is still the same, and that is any use of any medications in his history are what they are, and it doesn't change my opinion.
Q. Is there any literature involving the study of ALS that points to a higher incidence of ALS in athletes than non-athletes?
A. Yes. There have been studies that athletes seem to have a higher incidence of ALS. Again, those studies are based on interactions between behavior that may increase oxidative burden.
Q. Such as trauma?
A. Trauma. But also there is a -- when you exercise vigorously, there is an increase of oxidative stress in the body associated with vigorous exercise. If

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you exercise regularly every day, you up-regulate your body's basal levels of glutathione and other things that scavenge free radicals, and that helps to offset that.
But short bursts of vigorous physical exercise that are not accompanied by regular training can increase the oxidative stress in the body and may hasten the course of ALS.
Q. May or likely?
A. Likely could by the same mechanism as toluene. The increase of oxidative stress that is implicated in ALS due to this burst of physical exercise would interact with the disease. And again, these studies that find an incidence increase of a disease interacting with a specific behavior are more likely, actually, looking at something that is altering the clinical course rather than causing the disease.
And by the same logic that the toluene could hasten the course or Riluzole could slow it, it is just a matter of two plus two equals four or two minus two equals zero.
Q. By the same logic, you just said that vigorous exercise likely could increase oxidative --

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A. Oxidative stress.
Q. -- oxidative stress?
A. That has been shown. There has actually been some studies that have looked at vigorous physical exercise versus persistent vigorous physical exercise and shown that the acute physical exercise causes an increase in oxidative body burden. Eating food causes an increase in oxidative body burden, everything we do.
But, obviously, the body tries to adapt to its burden. And if it can adapt, then the body functions. If it can't adapt, if that ability to adapt is exceeded, then you have a hit, what I will call a hit, meaning damage. So there is this interaction constantly. The body is constantly interacting with its environment. It just doesn't live in a vacuum.
Q. What I am trying to ascertain is is it your opinion that an increase in oxidative stress likely could hasten the onset of ALS or the progression of ALS or likely does hasten the onset of ALS or the progression of ALS?
A. Likely does.
Q. Based upon?

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A. Based upon what is known about the mechanism of action of ALS, the progression of neurodegenerative diseases in general, and how the body is damaged by oxidative stress. Oxidative stress causes something called lipid peroxidation, which alters the membrane of a cell. It is particularly susceptible in the nervous system. This increase in lipid peroxidation can lead to cell death, and ultimately contribute to the progression of ALS, and ultimately contribute to death in general in just everybody.
So we know a lot about the role of oxidative stress in aging and in disease, and it comes up from every angle. It is just a fact of life. And some things exacerbate it, and some things minimize it. We are always looking for ways to minimize it from a treatment standpoint because we are faced with it as a common denominator.
Q. Given the studies that prove a higher incidence of ALS in athletes, did you attribute any significance to the fact that Mr. Allen was obviously an athlete and continued to be one well into his midlife?
A. Yes, I did. I considered that as well.
Q. What significance did you attribute to that in terms of either causing or hastening ALS?

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A. Again, it didn't contribute anything to causing, but again I considered the fact that he was athletic to his ALS, and I concluded that the contribution was not as remarkable as the toluene exposure.
Q. How so?
A. How so? The toluene exposure in his case was quite, for someone with a neurodegenerative disease, obviously high enough to cause him problems acutely and, therefore, would have impacted the progression of his ALS.
As an athlete, what we don't know for sure about him is whether or not he was having bursts of exercise or whether or not he was chronically exercising. But given the fact that he was a coach, a football coach, we would expect that he was, you know, a regularly-exercising individual. And meeting with him and seeing him, even when he was sick, he was still physiologically a very strong --
Q. Fit?
A. Fit. Even when he was sick, he still was not someone who was not fit.
So it gets back to that question of what exactly is the type of exercise that would have to hasten ALS. And so again, I come back to the fact

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that you take your patient as you find them, and I think that his exercising could have been a contributing factor, but I certainly think that the toluene is an important contributing factor, more so than the exercise level, because the toluene is a known toxicant and the exposure occurred at levels that caused, as least, acute levels of toxicity.
MR. MAHONEY: Let's go off the record.
(Discussion off the record.)
MR. MAHONEY: On the record.
BY MR. MAHONEY:
Q. I just asked you about the fact that there are studies that prove that athletes have a higher incidence of ALS and how you determined whether or not that was significant. And I think you told -- significant in a diagnosis of ALS or a hastening of ALS. And I think you said that you had considered it, but given the amount of toluene that he was exposed to, you thought the toluene exposure was a more significant contributing factor; is that right?
MR. GOTZ: Objection.
A. That's correct.
Q. But the only quantitative --
MR. MAHONEY: Well, strike that.

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Q. There is no quantitative assessment of how much toluene he was exposed to; is that fair to say?
A. That is fair to say.
Q. And your opinion with regard to his exposure is strictly limited to the acute symptoms that you found that he suffered from following the floor refinishing; is that right?
A. That's correct. But can I qualify that?
Q. Not that one, no.
I want to ask you some other ALS-related questions, obviously.
Do you agree that studies looking at an association between the prevalence of incidence of ALS have failed to find a significant association between exposure to any specific neurotoxic chemical and the occurrence of the disease?
A. Yes.
Q. Do you agree with the statement that the association between neurotoxic chemical exposure and age of onset of ALS is more --
MR. MAHONEY: Strike that.
Q. Do you agree with the statement that the association between neurotoxic chemical exposure and the age of onset of ALS, which is more likely to occur, has not

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been extensively studied?
A. Yes. I would agree that that area is emerging now because we have discovered after so many years of beating it up from the wrong direction that we have been looking at it the wrong way.
Q. Do you agree that the literature as it relates to ALS indicates that 90 percent of ALS cases are not familial?
A. Yes.
Q. And that sporadic and idiopathic account --
MR. MAHONEY: No. Strike that.
Q. And that 90 percent of the cases are sporadic and idiopathic; is that right?
A. The majority of case are sporadic and idiopathic, yes.
Q. Do you agree that there is epidemiological data that indicates that incidence of ALS increases with age, but sporadic ALS commonly occurs between the ages of 40 to 60 and can occur between 40 --
A. Yes. There is literature that shows the age of onset can be younger than 60. The mean age of onset is usually closer to 60, but there is obviously variance in the age of onset of a disease.
Q. Let's talk about the age of onset issues. Your

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opinion is that the exposure to toluene as found in the refinishing products at Holy Cross hastened the overt symptoms of ALS and the progression of the disease; right?
A. Um-hmm.
MR. GOTZ: You have to say "yes."
A. Yes.
Q. What is your opinion with regard to the progression of ALS had Mr. Allen not be exposed to it?
A. Then he would still have all the other factors in his life playing a role in his onset. There is several things I take into consideration in my opinion. One is his whole history, which would include use of any medication, his level of physical exercise. All those things were considered, and then the exposure.
There is no doubt in my mind that Coach Allen would have developed ALS had he not been exposed. What I can tell from what I know from my knowledge in this area is he was exposed to a chemical that shares mechanisms in common with ALS, number 1. Number 2, his symptoms of ALS emerged after he was exposed, not before. Number 3, he did develop ALS on the young end of the spectrum.

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Those factors combined are considered in my opinion as such collectively and, as I said before, I take the patient as I find him. I have identified all the factors in his life, and I find no other factor that stands out as strikingly as does the exposure that occurred during the refinishing process, and I find no other factor that anyone involved in ALS research would not recognize as a sharing of mechanisms that we look for when we are trying to discover pharmaceuticals.
So it is just impossible for me to assign a higher value to any other thing in his life than that exposure and his genetic predisposition to develop the disease. Those two factors just came to collide.
Q. Do you have an opinion as to the time that he would have developed ALS had he not been exposed to toluene?
A. Yes.
Q. What is that?
A. I think he would have been considerably older. I think -- the mean age of onset we would expect to be closer to 60. It is hard to say for sure how many days, weeks, months the toluene contributed, but I

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think it is fair to say that he got it at least, you know -- and I don't want to give an exact number.
Q. How about a range?
A. I would say anywhere from two to five years earlier, maybe, more than he would have otherwise. You look at the standard deviation from the mean. You look at the age that he got it at. And you have got this window in there that is pushing it down. I, like I say, I can't give you an exact number, but it would be --
Q. What is the standard deviation from the mean?
A. I don't remember off the top of my head. I think one standard deviation is like five to seven years in ALS. And two standard deviations would be like right about where he is.
Q. So the mean was, what, 60?
A. 60s.
Q. So 5 to 7 would be 55 to 53, on the low end, and the other end, obviously, but we are going to concentrate on the low end. And two standard deviations would be 10 to 12 years?
A. Would be about where he is.
Q. So do you have an opinion --
MR. MAHONEY: Well, strike that.

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Q. And he got it, what, at 45?
A. 45. I think it was 45.
Q. How old was he when he passed?
A. How old was he when he passed?
Q. He was 48 years old when he passed in 2004.
A. 48, so he was -- because he just turned 45?
Q. His date of birth was December 7, 1955.
A. So was he 44?
Q. What is your opinion as to when he was, I don't want to you use the adverb "officially," but officially diagnosed with ALS? Was it Doctor Polkin, Doctor Chad, or Doctor Russell?
A. I would have to go back and look and see. Again, I think he was diagnosed with ALS before he was officially diagnosed with ALS, unfortunately, because of his wife.
I really feel that she was pressuring, maybe didn't want to, and was hoping for some other diagnosis. I think the physicians were leaning that way but not putting it in writing.
Q. I believe that the medical records indicate that Doctor Polkin, at least in November of 2001, made a diagnosis of possible ALS on December 2, 2001.
A. Um-hmm.

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Q. You remember that?
A. Yes.
Q. And then Doctor Russell, who he saw on January 22, 2002, made a diagnosis of widespread fasciculations, elevated CPK. What is CPK?
A. Creatine-phosphokinase.
Q. And left foot drop.
Doctor Russell said on that same day, which is January 22, 2002, that "it is unusual for motor neuron disease to present with fasciculations as the initial symptoms."
Do you agree with that?
A. No.
Q. Why not?
A. Because there is reports where the fasciculations are presented earlier in the disease, so I don't -- I don't know why he said that, quite honestly.
I mean a patient could present with fasciculations, and fasciculations are a common manifestation of ALS. So I really can't quite understand that. I don't know.
Q. In any event, he appears to have been about 45 years old when the diagnosis was made.
A. Um-hmm.

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Q. So you said that the standard deviation was five to seven years. So it is your opinion that given that he eventually would have succumbed to ALS that the onset would have occurred approximately 8 to 10 years later?
A. That would have been barring, you know, nothing else happening to him in the mean time. I mean it --
Q. So you can't say with a reasonable degree of scientific certainty?
A. Well, we don't know what would have happened. But if nothing would have happened to him, yes, he probably would have been 8 to 10 years older before he would have had symptoms.
Q. And in terms of nothing happening, you mean what?
A. No other exposures to chemicals, you know, he doesn't get a TBI or some other -- traumatic brain injury -- anything that could cause a loss of neurons. But if he had nothing happen in his life to dramatically alter the progression, you would expect him to be getting closer to the mean.
Q. What about the progression? We talked about the onset now for the past few minutes. What about the progression? Is it your opinion that the toluene accelerated the progression of his disease?

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A. Again, there is an abrupt hit period where there is this loss of neurons. So in that context, it is accelerating the progression at that point, and that moved the age on onset down.
After that hit, with nothing else there altering the progression, the damage is done, and there is no reason for it to continue to dramatically influence it. In fact, it would gradually trail off. Then he is on Riluzole trying to push it the other way.
So, you know, when you look at his time to death from the time that he became symptomatic and you look at the duration of the disease, how long he had the disease, did it progress more relentlessly after that? I would say that it wasn't as big of a factor as was moving it back to that point. I think once the cessation of the exposure occurred, the disease was exacerbated to that point and then progressed probably in a manner that was what it was again.
So it is, you know, there is some continued aggravation because you have killed some glutamatergic neurons. They have released their glutamate. That is going to maybe hasten the course

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some more. But now without that ongoing hit, once that hit stopped, the damage was done, and then it -- I don't see a big difference there when I look at the literature and I say, "How long should ALS take to take its course?"
And you look at how long he was symptomatic. It is not like it was very, very aggressive. It was aggressive, but I wouldn't say it was more aggressive than it would be within the confines of normal. I didn't see that as the case.
Q. What does the literature suggest with regard to overt symptomatology with the onset of death? How long a period of time is it on the average?
A. It is a couple years. Many times, it can be a couple years. It can be shorter, but it is two or three years. Some people live longer. Stephen Hawking is an example of someone who has been --
People succumb to the respiratory problems. People live longer because the respiratory problems are better managed. You know, they have swallowing difficulties. They have all kinds of problems that they succumb to. So the death in the case of ALS is just almost a crap shoot. I hate to say this, but if someone is managed properly, and some people just

live longer because they are getting better care. They don't -- but the respiratory problems are really the problem that really causes.

Q. So would you correct me if I am misstating your opinion? It seems to me that you are saying that the exposure to toluene accelerated his symptomatology but did not accelerate the progression of the disease and his ultimate passing. Is that fair to say?

A. I want to make sure it is said the way I would say it. In general, it accelerated the clinical course of the disease. Did it continue to accelerate the disease after it did its damage? Yes, but not as much as it did initially. So it would wane off with time. Its impact would trail off with the cessation of exposure.

So just like the benefits of Riluzole would cease when you stopped talking it, the damage would cease once you stopped being exposed. But the damage that was done would leave some residual sequelae, as would the protection of something like Riluzole would still have some benefit, but that would gradually tend to move back towards the norm of whatever the progression of the disease was

independent of the exposure.

Q. But the progression of the disease until his passing was basically an average progression; is that fair to say in terms of time?

A. I don't see it as being that much. It was aggressive, but I don't think it was exceptional. There are aggressive cases like that, and I don't know that you can say that it was more aggressive. But it is like a snowball going down a mountain. You add some mass, and it is going to pick up more mass more quickly.

But that effect gradually moved toward the norm again, so.

Q. You saw Mr. Allen in April of 2004, and then the opinion was written in December of 2005; is that right?

A. Um-hmm.

Q. And then in terms of the references for your opinion, neither you nor Doctor Jabre reviewed the material safety data sheets that were provided by Holy Cross by my client for the floor refinishing products. Is that fair to say?

(Handing document to the witness.)

Q. Here is it.

Prior to drafting that opinion, neither you nor Doctor Jabre reviewed the material safety data sheets that were provided to Holy Cross by my client for the floor refinishing products?

(Witness viewing document.)

A. So you are saying had we not seen any material safety data sheets at the time that this was written?

Q. Right.

A. There was things that were sent to me over time by Attorney Allen. I am not sure when that first box of stuff came. What I did have at that time was a knowledge of floor refinishing materials and these materials that are used in the process.

And so -- but did I have these material safety data sheets or other material safety data sheets? Because I had been sent material safety data sheets more than once, so I don't know exactly when those came.

Q. Okay. Well, the pages 4, 5, and 6 list all of the documents that you referred to?

A. Oh, these references here?

Q. Yes. In your report; is that right?

A. No. That only means that these are references that

support the science; not necessarily that support my knowledge of what was present.

Q. All right.

A. So this is not like footnotes that maybe you would use. They are --

Q. In any event, is the word "toluene" included at all in this opinion of December 5, 2005?

(Handing document to the witness.)

Q. Here. Why don't you take a look at it.

A. Sure.

(Witness viewing document.)

A. I don't see that it is in the report.

(Witness viewing document.)

A. I think at this point I simply focused on the mechanisms of neurotoxicants and didn't specify any specific agent in the report, and just on the general mechanisms at that point.

Q. Well, a few minutes ago, though, you said that there were other chemicals in the floor refinishing project that may have played a role, but not as significant a role as toluene?

A. Um-hmm.

Q. When was it that you gained that knowledge? Prior to December 5, 2005 or following December 5, 2005?

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A. So I was knowledgeable about the chemicals that were there either by conversations with probably Attorney Bell or Mrs. Allen, who may have been trying to get some information.

And then as far as the floor refinishing materials, when you start looking at polymers and solvents that traditionally go into varnishes and these kinds of floor refinishing materials, there is a short list that comes up all the time, and toluene is always on that short list. It is one of the principle solvents that is used in these materials.

So there is really no getting away from it, unfortunately. There is an effort in paints to get away from using toluene, but these varnishes, they are not just like latex-based, water-based paints.

Q. So you knew it prior to drafting the December 5th report?

A. I knew it from my experience in toxicology what chemicals, what polymers and solvents would be present in this kind of material.

Q. If that is the case, why didn't you refer to it in the report?

A. I just -- I just didn't. I think at that point I didn't want to go into that discussion at length.

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In this report, I spent more time explaining the mechanisms which I cover in there and showing how they interact specifically with toluene.

That is a very different report. That report is just staying that chemical exposures can interact with disease. That is it. This is explaining how the chemical exposure interacts with the disease. That is just saying they do.

And so those are just two very different documents. One is my basic opinion in this case, and the other is explaining how I arrive at my opinion and the science that I rely on in making that opinion.

Q. Do you know whether or not Doctor Jabre was aware of the presence of toluene in floor refinishing products in December 2005?

A. He would have had whatever information I would have had. So we both -- again, he is neurologist, so we work as a team. The environmental occupational neurology program is composed of several scientists and physicians that work together as a team. And some are expertise in molecular physiology, as is Joe, some are expertise in toxicology, some are expertise in neuropsychology, and we work together

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on these cases.

So whatever information one person has, the other person may have. But as an expert in electrophysiology, if Joe did nerve conduction studies and Joe gave me labs and said, "Look, Marcia, I got abnormal nerve conduction velocities," I would have to rely on Joe's work there. If someone is going to talk about the mechanisms of toxicity of toluene, then Joe differs to me.

So each one of us bring to the table our own experience. And so Joe would know the same information I would know, but he would not be typically discussing that beyond the same opinion as mine, as the chemicals can interact with the disease. But he wouldn't go into the mechanisms of toxicity. That is just not what -- he just wouldn't do that, no.

Q. The reference to the Haley study referenced in the 2005 report --

A. Yes.

Q. -- I just want to ask you some questions about that.

That is included as a reference in the report that we are talking about today that you prepared. What is the date on that?

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A. May or June.

Q. May of this year?

A. Yes.

Q. So let's call it the spring of 2007. So two years after the -- well, almost two years. About 18 months after the preparation of the December '05 report, you prepared a report for this case; right?

A. Yes.

Q. Why did you not refer to the Haley report in the report for this case when you did in the letter from 2005?

A. There is no particular reason. I was focusing my discussion in here on the mechanisms and how they interact. The Haley paper just is a more just general epidemiological question and just less important to understanding how this occurred.

Haley, you know, I don't exclude it from my position. It is just that they are two different documents. I am not going to just pump this full of references for any purpose, so.

Q. Well, in the 2005 report, you say at the bottom of page 2, "These findings collectively indicate that environmental factors such as exposure to neurotoxicants which increase oxidative stress

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and/or glutamate-medicated excitotoxicity can hasten the loss of lower motor neurons and the clinical course of ALS to thereby result in a younger than expected age onset of the disease."

And then in parentheses you have "Haley, 2003" after that.

Are you saying that Haley's study exactly says what you recite in that sentence that I just read?

A. Well, Haley looks at the incidence. He doesn't look at the age of onset, so we have to take that into consideration. But he notices that the subjects in his study are young. And he, at that time, was working within a realm -- where the science was in 2003 is very different than where the science is today and our understanding of ALS and Haley's purpose of that paper. But the observation that Haley made in that paper was that these exposed soldiers developed ALS younger.

This gets back to what I was saying before about incidence and a prevalence of disease. When people are exposed to chemicals and develop the disease younger, that is because some of those people would have died before they got overt

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symptoms had they got it at the mean age of onset. So they wouldn't have been included in those studies later on.

So when you push the disease younger, you seem to increase the incidence and prevalence. It is an artifact of making it happen younger that is related to the fact that people haven't died of something else before they develop clinically overt symptoms.

So it is easy to misconstrue that observation as meaning that the exposure is causing the disease or somehow causing an increase in the incidence, when really it is just unmasking the disease and making the numbers artificially inflated.

And the studies that are emerging and the direction that the neurodegenerative research is going today are focusing more on that. We have gotten away from this old idea of counting heads. For 20 years, people have been counting incidence and prevalence of Parkinson's disease and ALS and have been getting nowhere. That is why when all these studies come back, one finds one thing; one doesn't find it. You are looking at the wrong

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parameter.

Q. Do any of these neurotoxicants that are referred to in Haley include toluene?

A. Most of these soldiers were probably exposed to jet fuels, which could have included and would have included toluene and long-chain and short-chain hydrocarbons. They were exposed to pesticides. They were exposed to diesel fuel. I am pretty much familiar with the Gulf War story because of my instances with the VA, and they were exposed to all kinds of different chemicals depending on their job tasks and what they were doing over there in the field, so.

Q. Does Haley specifically cite toluene as a causative neurotoxin that results in the onset of ALS in a younger than expected age?

A. I would have to look at the paper, but I wouldn't think that he says toluene specifically in there. He probably just looks at pesticides and other chemicals that were in the environment over there.

Q. He also goes on to say, according to you from the 2005 paper, that, "ALS patients exposed to neurotoxicants at sufficient concentrations and for sufficient durations can be expected to manifest

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symptoms earlier and experience a more severe and rapidly progressing clinical course."

Do you recall that?

A. Um-hmm.

Q. In fact, that is what you and Doctor Jabre wrote on page 3; is that right?

A. Um-hmm.

Q. What were the sufficient concentrations, number 1, and what were the sufficient durations, number 2, that he ascribed to the expected manifestation of symptoms earlier?

A. So let me look at that. So you are citing -- where are you saying this was?

Q. Top of page 3.

A. Top of page 3.

(Witness viewing document.)

A. So that is my opinion based on the observations of these two studies that show that these subjects developed the disease earlier. You know, it is not uncommon --

Q. Can I just ask you? Do you quantify the sufficient concentrations or sufficient durations that are necessary?

A. No. Because sufficient means just that.

Sufficient.

It depends on the chemical. Some chemicals are more toxic than others. For example, we know with gamma-diketones, like n-hexate is metabolized 2, 5-hexanedione. The different gamma-diketones are more toxic than others, even though they are related chemically.

So you talk about sufficient concentrations and sufficient duration. It depends on the toxicity. A more toxic compound can be exposed to for a shorter duration and have a more significant effect. A less toxic compound, you would need a longer duration of exposure to have a significant effect. So these have to be taken into consideration.

Xylene it much less toxic than toluene. You would have to be exposed to it at higher levels for a much longer period of time if you are going to see any clinical manifestation.

So this is -- these statements are explaining in the context of if the concentration is high enough and the duration is long enough for that specific compound, you can alter the clinical course of the disease. Obviously if the concentration is

really, really low and the exposure is very, very short, you are not going to have anything happen.

So if I just came in the room with a bottle of nail polish and said, "Here, smell the toluene," and then closed it right up, you are not going to have dramatic affect on the age of onset of a disease. But if I filled the room with toluene and caused you to lose consciousness, you are talking about a totally different thing.

Conversely, if I left you in here for three weeks and you are experiencing dizziness and headaches and other symptoms, that is very different than the other two extremes, so.

Q. Okay. So the sufficient concentrations and durations that you opine that Mr. Allen suffered from are, again, only based upon the symptoms that appeared following the refinishing, not in any quantitative amount that was in the air in the field house?

A. Unfortunately, no one measured those levels.

Q. So do you agree with me?

A. Yes.

MR. MAHONEY: Want to take a break?

MR. GOTZ: Sure.

(Recess taken at 2:40 p.m.)

(Recess ended at 2:59 p.m.)

BY MR. MAHONEY:

Q. You are not discounting the effect of toluene on the progression of ALS in Mr. Allen, but your opinion is that its major impact was the accelerated onset of ALS; is that right?

A. That's correct.

Q. Is there a specific amount of toluene that a person who is susceptible to ALS must be exposed to and a specific duration in order to incur this hastened onset effect?

A. Well, the minimal amount would be that which contributed to an increase in the body burden of free radicals.

Q. What is that minimal amount?

A. That would have to be ascertained experimentally.

Q. Has that been done yet?

A. I don't know if that has been done. It is known that toluene increase oxidative stress, but I don't know that minimal amount. There is a limit of the devices used in and the assays used to measure oxidative stress to some extent.

So you would expect that there is a

continuum from none to the maximum conceivable amount of oxidative stress you could possibly have, and that is contingent upon generations of free radicals, specifically, and the inhibition of the ability of the body to scavenge for free radicals, both of which could be modulated by neurotoxicants such as toluene.

So you have got an additive effect on those two perspectives that reach a critical mass. But the specific amount, you can't say X amount has to be there. Once toluene is in the body, this is its mechanism of action. You can expect there to be an increase in oxidative stress. You can expect there to be changes in neurotransmissions. As those -- just like with ALS -- as those start to reach a critical mass, you start to have the symptoms. You start to have measurable changes in the body burden of free radicals and the ability to scavenge free radicals. So it doesn't just go from zero to 10. There is a continuum, and --

Q. But the specific amount of toluene that is necessary to trigger early onset ALS has not been quantified yet; is that fair to say?

A. That is fair to say.

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Q. Can low levels of toluene involved in an indoor air exposure cause headaches and nausea and other similar symptoms?
A. Again, they have to be high enough to cause those symptoms. So when you say "low levels," 5 parts per million probably wouldn't cause any clinical manifestations.
Q. The OSHA standard is 200; right?
A. Right. But can I qualify that?
Q. Sure.
A. Because that standard was rolled back from 100 parts per million. So OSHA would like to see it at 100 parts per million, but they have to work to get that set back to what it was.
Q. Let's stick with the 100 parts per million. Can 100 parts per million cause headaches or other symptoms?
A. You would not expect to see symptoms at that level.
Q. Okay.
A. Obviously, if that was a level that would cause symptoms, then people that were working with toluene would feel sick all the time, and that wouldn't be a very desirable outcome.
Q. So previously -- well, currently, the OSHA standard is 200 parts per million; correct?

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A. That's correct.
Q. If you wouldn't expect to see symptoms at 100 if the OSHA standard is currently 200, is the same true that you wouldn't expect to see symptoms at that level?
A. No. Because that level is in the process of trying to be turned back to 100. I think that for some individuals who may have problems metabolizing toluene, you might start to see symptoms at lower levels.
Q. Are there any studies that have proven that exposure to 200 parts per million of toluene will result in symptoms of headaches and dizziness and nausea?
MR. GOTZ: Objection.
A. I think there is individual variance there. You can't say in one individual versus a group. On the average person, or in a specific individual? I mean, for example, a lot --
Q. Well, can you just actually answer the question that I asked? Are there any studies that indicate that exposures to levels of toluene at 200 parts per million will cause symptoms of headache, nausea, or dizziness?
A. Let me just refer to this document here to see what

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I had stated here.
Q. Sure.
(Witness viewing exhibit 2.)
(Discussion off the record.)
MR. MAHONEY: Can you read back the last question, please?
(The prior question was then read.)
BY MR. MAHONEY:
Q. Now you are referring to exhibit 2, your opinion in order to answer that question?
A. Um-hmm.
Q. What page are you on?
A. Page 30.
Q. What paragraph?
A. Paragraph 4.
"Echeverria, 1989, noted subtle acute effects to be associated with exposure to toluene at just below 75 ppm and above 100 ppm supporting the position that the guideline be lowered since the biological threshold of behavioral effects may be comparable with the TLV."
So the behavioral manifestations start to be measurable at around 75 parts per million according to Echeverria.

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Volunteers exposed to 200 ppm certainly report experiencing "mild upper respiratory track irritation."
Q. Where is that?
A. Three.
Q. Oh, above?
A. Yes.
So, you know, these are the studies that are out there. Obviously, you know, this is what it is. And I am, you know, this is the amount of data that is there. So you are asking me a question. I can only show you what has been done.
So we are in that range where symptoms start to emerge somewhere between 100 and 200 parts per million.
Q. So let's focus on paragraph three.
"Volunteers exposed to a 200-ppm concentration of toluene for eight hours experienced mild upper respiratory tract irritation."
Is there any document that says Coach Allen was exposed to eight hours of any volatile organic compounds resulting from the floor refinishing?
A. From the documents I have reviewed, he was in that building for quite a while. He was there throughout

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working, throughout the process. So I am under the impression that he was there at least eight hours a day, maybe longer.
Q. Is there any evidence that he experienced mild upper respiratory tract irritation?
A. Among the complaints? I have to get back to --
(Witness viewing document.)
A. -- I guess, the original documents.
Q. Page 7 and 8 were the clinical examination of Dan Allen.
(Witness viewing document.)
A. So he reported experiencing acute dizziness, headaches, and disorientation. Other people reported similar symptoms. We have to bear in mind that what people remember to report and what they talk about are the things that bothered them the most at the time. So he may have experienced and would be expected to have experienced upper respiratory tract irritation if he was experiencing dizziness and headaches and nausea, because those would have occurred at even higher concentrations.
Q. But in terms of the upper respiratory tract complaints, there is no evidence that he made --
A. He did not complain about that.

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Q. And there is no evidence that Mr. Bradley, who apparently was an assistant football coach at Holy Cross, complained of upper respiratory tract irritation either; is that right?
A. I would have to see his report.
Q. Here it is.
(Handing exhibit 4 to the witness.)
(Witness viewing exhibit 4.)
A. So he says he smelled and felt the effects of the fumes. He felt dizzy and suffered headaches throughout this period. You know, again, he is saying he smelled it. So obviously he was probably bothered by the fumes.
Q. What paragraph?
A. 15.
He reports the fumes. He says his wife came in and smelled the fumes and suffered headaches for more than a day and ran out of there. Different people respond differently.
Also, when you are exposed to these chemicals for more than a short period of time, your respiratory system desensitizes. So the acute irritant effects start to subside and become less pronounced with ongoing exposure. And you can

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actually read my paper. I have a publication on that.
And so the first day he may have been experiencing those respiratory irritant effects, but then maybe he got used to the smell, and it didn't bother him as much, and he just, you know, just lived with it. That is often what happens.
Q. Were there ever any complaints of mild eye irritation that Mr. Allen expressed?
A. Again, he doesn't report them specifically.
Q. What does lassitude mean? Dizziness? Vertigo?
A. It is sort of like a general feeling of --
Q. Malaise?
A. (Witness nodding her head.)
Q. Did he ever complain of any drowsiness or uncoordination immediately after this exposure?
A. I don't see that he did.
But dizziness borders on uncoordination. If you are dizzy, you may have problems with balance and walking, so you are right on it. Once you start having vestibular system problems, you are, you know --
Q. Now toluene can be found in many products; is that right?

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A. That is true.
Q. Did you inquire from Mr. Allen as to his exposure to any of those other such products that toluene could be found in?
A. Again, just, you know, asking him about his general occupational history, what he did, other jobs, did he work with chemicals at home, this kind of thing.
Generally, the background levels, does his wife use nail polish or something like that, the ubiquitous background level is not something that I would worry about. Beyond the fact that it is a part of life and we all live in this -- it is just -- I am looking for a major contributing factor in his history, not something that may be contributing but at an amount that is, you know, no different than going for a run around the block one day.
I am looking for a big hit, a big hit in time consistent with my dissertation research, consistent with other materials I have published, consistent with other work that is ongoing in neurodegenerative disease, that when you have got someone who has worked for a period with chemicals or worked in an environment where there is chemical

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exposures, I am taking this into consideration. This is more than you would get by just sitting next to your wife while she does her toe nails or something like that.

Q. Is it true that a viral infection can hasten the onset of ALS?

A. Again, there has been associations just as there has been with exercise between ALS and these things. You take the patient as you find them. I don't discount or exclude any of those factors in his case. I only demonstrate here that the exposure was one of the major contributing factors in his case.

He, you know, all kinds of things have happened in his life, so, you know, he is what he is. He did report having diarrhea and other symptoms while he was on vacation.

Q. In Aruba?

A. Yes. And we don't know whether that was a bacterial infection. We don't know what that was exactly, so.

Q. Let me ask you about that conclusion.

On August 17, 2001, stool cultures were tested as negative for bacterial infection by Doctor Polkin. Do you remember that?

A. Um-hmm.

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Q. And Polkin went on to say, "No infectious pathogen was identified."

Would that rule out a bacterial infection in your view?

A. At that point, there wasn't one that he could measure, but they still put him on an antibiotic, which would be used to treat a bacterial infection.

Q. Are antibiotics also used to treat viral infections?

A. They really are not designed to treat viral infections.

Q. Are they used to treat --

A. People will use them to ward off an opportunistic bacterial infection when someone has a viral infection. But other than that, they have no clinical value. They don't attack viral infection. They have no physiological ability to do that.

Q. Right. But they are used to treat viral infections?

A. To prevent bacterial infections. That is the only purpose, to prevent an opportunistic bacterial infection. That is their only value.

Q. So with regard to the complaint that he claims to have suffered from when he was in Aruba from July 23 to July 29 of 2001, did you arrive at any opinion as to whether that was a bacterial or a viral infection?

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A. I can only look at the fact that he had an infection, what is reported there. Certainly, if there is any kind of stress that the body experiences, is going to alter the course of a disease.

The question becomes as to how can I define mechanistically the role of that specific viral infection in the progression of his ALS. And it would be right now impossible for me to say that that specific viral infection hastened the course of his ALS.

Q. Why?

A. Why? Because I would have to determine mechanistically how that viral infection would hasten the clinical course of his ALS.

Q. And how would you do that?

A. I would look for the same thing I have done here, the point of interaction with the ALS and of that specific virus. So with toluene, I am able to show mechanistically how the two interact. I would have to do the same thing for that virus.

Again, I am not going to say that the virus does nothing, but to say specifically the

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interaction, I would have to know specifically what that virus was, specifically the mechanisms of action of that virus.

And viral infections as a rule are acting by a mechanism not related to glutamatergic neurotransmission, per se. They are acting by interacting with the cell's machinery in a way that is different from what a neurotoxicant does.

So again, I wouldn't exclude the viral infection from playing a role, but again, the exposure to toluene is very remarkable in his history and, you know, we can say he exercised, he ate X diet, he did all these things. I have to take him as I find him.

And I have got this one salient thing in his life that stands out that was not typical, and that is his exposure to a known neurotoxicant that occurred in chronologic relationship to the onset of his disease, that shared mechanisms in common with that associated with ALS, and that the exposure was documented, the levels that occurred were high enough to cause acute symptoms.

I have to ascribe a considerable amount of weight to the value of the exposure. And those

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other factors, I don't completely discount them, but I don't think they are as heavy of factors in this case.
Q. But you do recall that he was diagnosed with infectious gastroenteritis?
A. Yes.
Q. And you agree that ALS can be triggered by internal virus complications?
MR. GOTZ: Objection.
A. Again, there is studies that have associated ALS with quite a few different things.
Q. Okay. So when you say "quite a few different things," you mean viruses; right?
A. With running, with infection, with trama. You can look at all these things.
Q. Let's focus on viruses.
A. Sure.
Q. There are studies that say that ALS can be triggered by a viral infection; is that fair to say?
A. There are studies that suggest that, yes.
Q. And your opinion is that exposure to toluene was more remarkable than the viral infection, and, therefore, it is the toluene that hastened the onset of ALS rather than the viral infection; is that fair

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to say?
A. Yes.
Q. And you eliminated the viral infection as a potential trigger for ALS by what methodology?
A. I did not eliminate it entirely. I weighted it. I weighted it relative to the toluene, and I ascribe it considerably less value than the toluene.
Q. Because?
A. Because the toluene has a specific mechanism. The specific viral infection that he incurred is not something that I can say definitively, mechanistically causes a progression of ALS. And even though there is some increase in the incidence reported in some cases, the value of that in this case does not appear to be -- let's, for example, take a situation where someone develops Guillane-Barre Syndrome or something really substantial like that. Then you have got a really strong viral infection that could kill neurons. But this specific infection which did not cause him symptoms such as demyelination or something like that, it is difficult to say conclusively that it has greater value in this case than the toluene.
I think it is reasonable to say that the

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toluene continues to be the most salient factor in his disease. I cannot ascribe the same amount of value to that infection. I just can't see it as demonstrable mechanistically or in any other way as being the case. There is just no -- there is just nothing to substantiate that.
I can substantiate this. I can't specifically substantiate the role of that. And if I did, I think I would have to be speculating. I would have to be saying, "Well, there is some epidemiological literature that suggests this may be the case. So, therefore, all viruses can do this." That would be just like me saying, all chemicals can hasten the course of ALS.
Q. Isn't that what you said in your December 5th letter?
A. No. No. Not all chemicals. So, for example, if you read, it doesn't say "all chemicals," because some chemicals we know can slow the progression of ALS.
Q. You say, "These findings collectively," on page 2, "indicate that environmental factors such as exposure to neurotoxins" --
A. Neurotoxins, right.

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Q. So are you saying that all "neurotoxins which increase oxidative stress and/or glutamate-mediated excitotoxicity hasten the loss of motor neurons in the clinical course of ALS"?
A. In that case, yes, because they share a common mechanism.
Now, for example --
Q. Okay. Before you give me the example, what peer reviewed studies support that conclusion?
A. That neurotoxicants enhance ALS?
Q. Yes.
A. Well, we know that pesticides have been fairly well studied in animal models, superoxide dismutase animal models showing that this interaction occurs. I can't remember the exact references off the top of my head, but there are some in here that talk to this.
What is going on with Bob Ferrante and Flint Beal has looked at the interaction between pesticides and superoxide dismutase.
Q. I am talking specifically about ALS.
A. This is the only way to study this. You cannot give the poisons to the people to study them. So you have to use an animal model.

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If I am the FDA and I trying to develop a pharmaceutical, I just cannot go just give it to people before I put it in an animal. The same holds true for toxicology studies. We really have to, whenever possible, revert to the animal model. It is just unacceptable.

Q. Getting back to the viral versus toluene, there are a number of peer reviewed articles that suggest that a viral infection can trigger ALS; isn't that right?

A. This --

Q. That is a yes or a no.

A. This is looking at incidence and prevalence.

Q. Well, you either agree with me or you disagree with me. Are there a number of peer reviewed articles --

A. There are peer reviewed papers that show an association between viral factors and ALS.

Q. But there are not peer reviewed articles that show an association between toluene and ALS; is that right?

A. This is true. No.

Q. And yet you ascribe that toluene, without the benefit of a peer review article, to be the major predominant cause in the hastening and onset of ALS; is that right?

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A. That's correct.

And that is because I can show here a mechanism by which toluene can do that. And the incidence -- there may be that a viral infection mimics ALS and looks like the neurodegenerative disease.

What we don't know is are those cases -- for example, in Guam, there are these cases of ALS/Parkinsonism which exactly what causes them -- it looks like ALS, but it is not typical ALS. So when you see this viral infection relationship, you are talking about a situation where the virus may create a disease that looks very similar to ALS. We call it -- and that is a motor neuron disease, but it is not ALS per se.

And so therein lies the problem with the epidemiological literature, without a mechanism of action, just looking at the incidence and prevalence of the disease without the pathology to say this is absolutely not -- if a viral infection causes ALS, it goes back to the same thing I say about the toxicant causing a motor neuron disease by itself, then it is the result of viral infection. It is no longer a disease.

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And so you come back to the same argument. You either have a disease that is interacting with the environment or you have something else. You either have a toxic exposure effect or you have a viral infection or you have an interaction between the two.

And I cannot say based on studies of incidence and prevalence that this viral infection with a mechanism that I cannot clearly define as interacting with ALS can hasten the clinical course of the disease.

I can show this happens. It is irrefutable. I cannot say that that virus is hastening the course of the disease. And if there is an increase in the incidence of motor neuron disease, I cannot say for sure that that virus isn't causing a syndrome that looks like ALS.

MPTP is a neurotoxicant that causes Parkinsonism that is identical to Parkinson's disease, but it is not Parkinson's disease. Pathologically, the loss of dopaminergic neurons is similar, but it is a toxic effect. It is not Parkinson's disease. And that is the problem. I just can't go there. I just scientifically --

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Q. Earlier today, do you remember at the start of the deposition we were taking about this latency period and this period of subclinical ALS that you believe Coach Allen had prior to his exposure, his alleged exposure to the toluene in the floor refinishing?

A. Um-hmm.

Q. And you said that you -- correct me if I misstate your testimony -- that given that there is really no way to test whether someone is subclinical because they don't have any symptoms, there is no way to know how long they have been subclinical or how long ALS has been latent in their body. Is that fair to say?

A. Yes. Because some can progress very slowly, such as is the case with Stephen Hawking. He has been around for years, so.

Q. Then what I want to ask you about is, if you refer to the December 5 letter of 2005, exhibit 7, on page 3. If there is no way to know how long a person is subclinical or how long ALS has been latent, how do you arrive at the opinion in number 2 here in this last paragraph, "that Coach Allen developed symptoms of ALS in chronological relationship to this specific exposure"?

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How can you define the chronological relationship if you don't know how long he was subclinical?
A. He doesn't matter. He had the exposure and then the symptoms emerged. I said he developed symptoms in chronologic relationship. I didn't say he developed subclinical problems. He developed overt symptoms.
Q. What is the specific chronological relationship you are referring to?
A. The ALS symptoms emerged after the exposure to the solvents.
Q. What study can you point to that has been peer reviewed that shows that after an exposure to toluene he will develop symptoms in a certain amount of time?
A. There is no studies to show that at this point in time. But we can say that if the exposure occurs before the onset on the disease, and the exposure is through a neurotoxicant, then it can interact.
If the disease occurs before the exposure, and then an exposure occurs, it can also interact. And as I said, if he had continued to be exposed after he was clinically overt, his disease would have progressed much faster.

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You asked me before do I think it unmasked it and how much do I think it contributed to the progression once it was unmasked. And I stated that once the cessation of exposure occurred, the impact of it did not progress at the same rate. But if he had been continued to have been exposed, you would have expected it to go even faster. That is the exact logic of why we give Riluzole. We are trying to give something that will slow that progression after it has emerged.
So the only thing we can say for sure is that he was asymptomatic before the exposure. He is exposed, and he becomes symptomatic. I have a chemical he was exposed to in concentrations high enough to cause overt symptoms, and the chemical has mechanisms of toxicity that have been implicated in ALS.
Q. Earlier, we were taking about the lack of references to toluene in that December 5th report. But in looking on page 3, the fourth line from the bottom, you stated, "Several of the chemicals Coach Allen was exposed to are known to be neurotoxic, for example, toluene."
So you did mention it in that letter, so the

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record is clear. But just so the record is equally clear, you had not reviewed the MSDS sheets to affirm that toluene was present in the chemicals that he had allegedly been exposed to?
A. Again, I don't know. I don't recall the exact date when I received the material safety data sheets that were sent to me originally by Bonsignori or Alan Bell. By the time I wrote this, I may have received them. Otherwise, I would have been told by them that they had them and they knew that it was there, even if I did not have them in my possession yet. I must have -- either I received information from them through some information that was disclosed -- I didn't make that up, so he had to have disclosed that to me somehow.
Q. Earlier we talked about trauma potentially triggering ALS. Do you recall that?
A. Yes.
Q. And there are studies that suggest that trauma can trigger ALS symptoms; is that right?
A. Yes.
Q. Do you know whether or not those studies indicate how long after the traumatic event these symptoms of ALS are manifest?

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A. Again, it would depend on the relationship of the progression of the disease to the time and the magnitude of the hit.
So, for example, if he had an head injury at six years old, it may still contribute to the age of onset of ALS, but that interaction wouldn't occur until you are 45 or 50 years old. So you wouldn't know that; you wouldn't see that. If you had the trauma at 45 years old, that interaction may be almost instantaneous because the loss of neurons had reached a point where you would push it over the edge by losing just a few more where the symptoms would become overt.
So that interaction is contingent upon when it occurs in relation to the volumetric loss of neurons associated with the progression of the disease.
Q. If he had incurred trauma approximately four years prior to being diagnosed with ALS, would you attribute any significance to that trama, for example, a rotator cuff tear?
A. Well, you are talking about a possible peripheral nerve injury, and, you know, if that resulted in neurological dysfunction -- now when you say

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"trauma," trauma doesn't just mean a punch in the stomach or a rotator cuff or a broken thumb. We are talking about trama to the nervous system. We need to traumatize the nervous system. We need to ask, you know, where is this trama? Is it going to directly affect the nervous system? And to what extent?

Q. What is your opinion with regard to a rotator cuff tear? Does that affect the nervous system?

A. It can, but it doesn't have to.

That injury might have exacerbated the symptoms of ALS in his arm, in the affected arm, but it would not be expected to exacerbate them globally because the impact would be — that is a local injury. It is like if you have a stroke, there is a loss of neurons here. But toxicants bathe the brain; they bathe the nervous system. Their effect is diffuse.

So when you see an interaction like that, you expect there to be a focal interaction, not a diffuse interaction.

Q. But after the onset of ALS and the development of fasciculations, are they usually bilateral fasciculations, are they usually upper extremity or

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lower extremity, or can you start with one extremity?

A. Yes. They emerge different places along the course of the disease. Some people present initially with bulbar symptoms; some people present with lower extremity symptoms; some people present with upper extremity symptoms.

So the presentation -- and this again probably reflects the focal losses of neurons that go on in the body just due to whatever happens in that person's life and how they interact.

If you have carpel tunnel syndrome and then you are exposed to toxicants that kill a nerve, that can make your carpal tunnel syndrome worse. So any interaction, any point of interaction, you are going to have greater manifestations in that region versus another. There is just -- nothing happens in isolation.

Q. Is your conclusion that toluene hastened the onset of ALS a differential diagnosis?

A. The differential diagnosis typically -- when we think of a differential diagnosis, we are differentiating one disease from another. Here, the differential diagnosis would be ALS versus

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Parkinson's disease or some other neurodegenerative disease. The question here is not "Is this ALS?", but did the chemical exposure somehow interact with ALS in some way. So the differential here would include other motor neuron diseases that might initially look like ALS. The bulbar presentation, the clinical course that I saw in him by the time I saw him argues that this was, in fact, idiopathic ALS. So the differential was, in my opinion, satisfied at that point.

And the question was only: Did in some way this exposure history interact with the disease process? And that is the only opinion I have, is that the exposure interacted with the disease process.

Q. You said the differential was ALS versus Parkinson's or some other neurological disease?

A. I was just giving that as an example.

Q. Why wouldn't the differential be -- when we are focusing on the impact of toluene on the onset of ALS, why wouldn't the differential be on any other environmental cause, trauma, viral? Why wouldn't that be the differential?

A. Now if you are asking what factors could influence

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age of onset, then I looked at all the factors in his history, I looked at his working in fields where maybe there were pesticides. I looked at his exercising. I looked as his viral illness. I looked at all these things. And I looked at in his life history in his case, what is the most substantial factor that could contribute to the disease that I am confident was idiopathic ALS, and the only factor that I found that was irrefutable was his exposure to chemicals.

As I said, I am not saying the chemicals caused ALS. I am not saying that viral factors caused ALS. I am not saying that running causes ALS. All these things collectively can contribute and modify the course of the disease in various ways. But among the factors in his life that were most likely to have a marked impact on his age of onset is this factor. The position of the Occupational Safety and Health Administration, the exposure levels that he was exposed to causing overt symptoms that he complained of, all of these factors taken together leave me unable to state with a reasonable degree of medical certainty that toluene did not play a role in this case. It absolutely

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did.
And in my opinion, the only argument is, you know, to what extent. Not if, but to what extent. And I think that it is a considerable extent. I just do not believe, given everything that stands in front of me, that this guy would have developed ALS two standard deviations below the mean but for this exposure.
Q. How do you define "considerable extent," the toluene's effect on the onset of ALS?
A. Considerable extent in that the compound is known to interact with the disease. When you are saying "considerable extent" --
Q. I am using your language. You said at the --
A. Reiterate on what I said so I make sure I use it in context.
MR. MAHONEY: Could you read that back?
(The previous testimony was then read back as follows:
"Answer: All of these factors taken together leave me unable to state with a reasonable degree of medical certainty that toluene did not play a role in this case. It absolutely did.
And in my opinion, the only question

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is, you know, to what extent. Not if, but to what extent. And I think that it is a considerable extent. I just do not believe, given everything that stands in front of me, that this guy would have developed ALS two standard deviations below the mean but this for exposure.")
BY MR. MAHONEY:
Q. So what I am asking you is what you mean by "considerable extent."
A. Considerable extent, that is when you look at the mean age of onset of ALS that he was below that in a marked way. And so if he developed ALS at 55 years old and had this exposure history, I wouldn't be sitting here today. This --
Q. Why?
A. Because I would say that the exposure -- let's say -- let me rephrase that.
If you came to me and said, "I have a patient with a history of exposure to toluene and he developed ALS at a normal age," and you said to me, "Did this exposure to toluene markedly alter the course of his ALS?"
I would say, "Well, yeah. But this guy probably would have gotten it at 75, and now you

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have moved him back to the norm." So, you know, you probably wouldn't be able to do anything with that.
Q. Legally?
A. Legally, right.
Q. From a damages perspective?
A. Right. But when he is younger than the mean, then this has had an impact on his life. In medicine, we deal with -- disease has to impact you in some way. You know, people prescribe antidepressants today like they are candy, but if someone isn't having depressive symptoms that are interfering with their activities of daily living, then you shouldn't be prescribing them antidepressants.
You should be saying, "Oh, you feel depressed, well, that is too bad." But if it is not interfering with your activities of daily living, it is not technically depression. When you look in the DSM-IV and you look for diagnosis, something has to impact your livelihood; it has to impact your ability to function.
In this case, I was brought here because this impacted this man. My opinion would be the same even if that guy died at 60 instead of 75 and had this history of exposure. I would still say the

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same thing. But you wouldn't have bothered to depose me in that case. So that is my point. So it doesn't change. The impact in this case is problematic. The impact --
Q. But it is not an early onset in the other case; is that what you are saying?
A. It is still an early onset for that individual, but it is not impacting him. It is impacting him personally, but no one is going to go after somebody for that because what are you going to say about it. So it doesn't take away -- when I studied Parkinson's disease in patients, I saw the average age of onset got younger. Some people were moving down from high down, but overall the whole mean moved down. You are taking that mean and you are moving it down.
So this guy is just, the N of 1, he has moved down from where he was to here. Somebody else has moved down from where they are to here. But it may not result in a lawsuit, and I wouldn't be here, because -- I wouldn't be here. But it wouldn't change my opinion in this case.
Q. I just want to go back to the range of years that you believe that this early onset affected.

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Before we broke a while ago, at first I thought you said 2 to 5 years, and then you spoke about 8 to 10 years. Now you are talking about two standard deviations.

When you spoke about standard deviations before, I thought you were referring to plus or minus the years that could deviate from the onset of ALS.

A. From the mean.

Q. From the mean?

A. Right. That is still the standard deviations.

Q. So when you say standard deviation, what is the year range that you are referring to?

A. I have to go back and look at those numbers --

(Witness viewing document.)

A. -- to remember if it is 5 or 7 years that is the standard derivation in ALS. I have to go back and look at some of the other studies. But for argument sake, let's say it is 5 years, so two standard deviations would be 10 years.

So if the mean was 60 and the standard deviation is 5 years, two standard deviations bring you to 50. If you are less than 50, if you are 44, you are six years younger than two standard

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deviations from the mean.

Even though some people can develop ALS young than that -- Stephen Hawking developed it even younger than that -- the standard deviation, you go back one or two standard deviations from the mean, and then you see how much younger he is than that.

So if we concluded that the standard deviation was 5 years and the youngest you would be expecting him to develop it is 50 and he gets it at 45, that is five years younger than two standard deviations from the mean. So that is my summary of that.

Q. So what is the age range that in your opinion this exposure to toluene adversely affected the onset of ALS and detracted from his quality of life?

A. Again, using that same model, I would say it is 5 years, and I have to go back and look at the exact numbers for the standard deviations from some of the studies published, but I think from a broad perspective, that is pretty close.

Q. Is that in your report somewhere?

A. It may be in one of these reports.

(Witness viewing exhibit 2.)

Q. What page are you on?

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A. 33.

I don't say that here. We would have to go look at these references to see exactly what two standard deviations are from them. Let's say it is 5 to 7 years. It could be anywhere from 1 to 5 years difference that he is below two standard deviations, using those numbers as an example, but I just didn't write it in here. I gave the mean, but I didn't give the standard deviation. So I don't know those off the top of my head. I do believe it is around 5 years, if my memory serves me right.

Q. Are you able to say with a reasonable degree of scientific certainty that the exposure to toluene in 2001 deprived him of a quality of life that he likely would have had from age 45 to 60 when he eventually would arrive at the mean for symptomology of ALS?

MR. GOTZ: Objection.

THE WITNESS: Should I answer that?

MR. GOTZ: Yes.

THE WITNESS: I do think that because he got the disease younger, he was impacted. What his life would have been like had he developed overt symptoms at 50, you know, obviously sooner or later, this guy

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was going to end up in the same place.

So, you know, it deprived him, in my opinion, of some quality of life. I can't say the specific impact of that. I can just say that, you know, if he would have gotten it five years later, he, you know, probably would have had five more years of time. He still would have died. He still would have suffered. So nothing would have changed in that regard. It is just when it occurred, as I said before, not if.

BY MR. MAHONEY:

Q. Do you agree or disagree with this statement: "There is a paucity of data regarding behavioral neurological effects of exposure to low levels of toluene, the extent and nature of the neurobehavioral effects, and the threshold of exposure to toluene at which such effects may occur"?

A. To the low level? Say that again.

Q. Sure.

"There is a paucity of data regarding behavioral neurological effects of exposure to low levels of toluene, the extent and nature of the neurobehavioral effects, and the threshold of

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exposure to toluene at which such effects may occur."
A. Yeah. I would like to see more. I can certainly say that. But, you know, there are recent studies that are looking at lower levels. There is a recent study with mice using 250 PPM of toluene with like a three-month exposure --
(Witness viewing document.)
A. Maybe not even that long. People are getting at using these models more consistent with lower levels that occur in occupational settings. You know, the field of -- it just never stops. You know, you are always having to -- everyday, I go home and I check the literature to see what else is out there. But there is not as much as I would like, if you want my opinion.
Q. "Exposure to toluene causes progressive development of central nervous symptom dysfunction with acute symptoms of drunkenness, dizziness, euphoria, delusion, nausea, and vomiting, and chronic symptoms of disorientation , confusion, headache, blurred vision, reduced speech, muscle coordination, ataxia, depression, reflexes, and" --
A. Nystagmus.

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Q. -- "nystagmus." That is according to the Oliver study. Are you familiar with that? 1977, Abusive solvents.
A. I have probably seen it before. Off the top of my head, I don't remember.
Q. I think you said earlier that toluene also causes neuropsychological damage involving the -- well, cognitive loss; is that right?
A. That's correct. I have reported on that. I have a peer reviewed publication on that.
Q. But in all of the medical records that we have from Mr. Allen, there is no evidence that he suffered any cognitive impairment, I mean even up to the time that you saw him?
A. I have seen, you know, when a patient has a --
Q. Is that right? There is no evidence that he suffered?
A. He didn't complain of anything. I will say that. He didn't complain about feeling any respiratory symptoms either, but that doesn't mean he didn't experience them.
Q. But he saw two neurologists. He saw Doctor Russell and Doctor Chad, and neither of those gentleman suggested that he sit for neuropsychological

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testing?
A. You wouldn't pick up in a cursory type of examination that happens during a normal neurological examination. You could not detect subtle cognitive impact of exposure to toluene.
And in addition -- and let me just qualify this further. He had -- we are talking about a situation where toluene is interacting with a neurodegenerative disease. The cognitive problem, you are talking about toluene acting on the normal functioning part of his brain. So the impact there is going to be considerably less dramatic than the impact on the abnormally-functioning part of his nervous system.
So part of the reason that he may not have experienced problematic cognitive issues, even though that can occur, is because that part of his central nervous system was not as vulnerable to the effect. And that is the explanation for the dichotomy here. And it is not to say that he didn't have any problems, subtle problems, but he -- they would not have been expected to be as bad. And in addition, given what was going on with the rest of his nervous system, even if he had them, they would

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have taken a back seat to what was going on.
In a cursory neuro exam that you do in a doctor's office, giving someone a bedside neuro exam for cognitive dysfunction is not going to reveal the subtle deficits that could be associated with these kinds of levels of exposure, even if they had occurred.
Q. Let's assume that that is true, that a cursory neurological exam wouldn't have revealed it. His wife was a registered nurse; is that right?
A. Yes.
Q. Obviously, she had some medical training; right?
A. Um-hmm.
Q. And there is no evidence that she ever mentioned that she noticed, subtle or not, any cognitive deficits from her husband; is that right?
A. Obviously, she is not complaining about them, no. But, again, the fact is that the rest of his brain, just like the rest of his body, was not as vulnerable. We are talking here about a chemical that can interact mechanistically with the mechanism of action of the neurodegenerative disease process.
If you take that same chemical in that same level and put it on a normal-functioning neuron,

okay, and the impact is inconsequential. It is nothing. It is trivial.

The problem is you interact it with a dysfunctioning nervous system or a dysfunctional part of the nervous system, and the impact is tremendous. And again, his wife was so preoccupied with what was going on with him overtly, that even if he didn't remember where his keys were by that point, she was probably getting them for him by that point.

Q. But you are speculating now?

A. I am speculating now. But I just don't see that even if he had subtle cognitive problems that they were on the forefront of what he was worried about at that time. So what I am saying is it is not to say that he may not have had anything, but his brain would have been more resistant, the normal parts of his brain would have been more resistant to that problem.

And in addition, given the magnitude of the overt manifestation he was experiencing, it just may not have been much of a priority even if he had subtle problems.

Q. Are you familiar with the classifications regarding

exposures to volatile organic compounds that are defined as primary exposure and secondary exposure?

A. Yes. I have heard of these terms.

Q. Would you agree with this: "Primary exposure occurs when an individual is directly exposed to a high concentration immediately after application, and a secondary exposure occurs when an individual is exposed but does not directly participate in the manufacturing or use of the product"?

A. Yes. Those terms are reasonable to use.

Q. So in this instance, how would you define Mr. Allen's exposure, primary or secondary?

A. Unfortunately, given the fact that he was in the environment where the chemicals were being used specifically, even thought he wasn't involved in the application process, he was exposed to the chemicals as if he were a worker because he was there on the site.

The secondary exposure would be more of the situation where a person came into the room, entered, and left, and didn't actually stay there and be in that environment.

Let's say you are working here with a bucket of n-hexane, and I am sitting next to you while you

are working with it. And you have got on gloves and all these things, and I am not working with it at all. I am sitting right next to you. By that definition, I would have a secondary exposure and you would have a primary exposure even though you have protection from dermal absorption and I had no contact with it and the only route of intake we both had was via inhalation. That definition would define me as secondarily exposed. Yet I am in the same room, I am the same distance from the bucket, my exposure is the same. So that definition is not -- you don't interpret it literally. You have to put it in context with --

Q. Is toluene an isocyanate?

A. No. There is toluene diisocyanate, but toluene itself is not an isocyanate.

Q. Was there toluene diisocyanate in the floor refinishing products?

A. There were diisocyanates in the floor refinishing products.

Q. Did the diisocyanate have any effect on the early onset on the Lou Gerhig's Disease?

A. Diisocyanates are considered sensitizers. People can develop occupational asthma and other problems

in relation to their exposure to them. There is no evidence to demonstrate conclusively in the literature that they could have enhanced glutamatergic excitotoxicity. That doesn't mean that they don't. It just means the studies haven't been done.

If you want, we can do those.

Q. Just like this one.

MR. MAHONEY: Let's take a minute.

(Recess taken at 4:01 p.m.)

(Recess ended at 4:16 p.m.)

BY MR. MAHONEY:

Q. Doctor Ratner, is there one scientist that you can name who has published an opinion that toluene accelerates the onset on ALS?

A. No.

Q. What other neurodegenerative diseases that share the same common pathways are accelerated by toluene other than Parkinson's and ALS? In other words, are there any others?

A. Well, any neurological disease can be exacerbated by exposure to a toxicant. I mentioned before if a toxicant caused peripheral neuropathy, say n-hexane, for example, causes peripheral neuropathy, and you

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had carpal tunnel syndrome, and you lost some nerve fibers in your median nerve as a result of a toxic exposure, that would exacerbate your carpal tunnel syndrome.

So any preexisting neurological disease or disorder can be exacerbated by the exposure to the neurotoxicant, so the weakest point is the most vulnerable point. So that is just a general rule of logic. It has nothing to do with -- it doesn't require any publication. It is just a fact. If I lose a neuron due to a toxic exposure and I have lost a neuron due to a compression neuropathy, they are additive. It is just simple math.

Q. Can Mr. Allen have had symptoms from dozens of other chemicals, the dizziness, the nausea, and the other neurodegenerative conditions?

A. As I state in my affidavit, I use toluene as the example. The chemicals to which Mr. Allen was exposed have not been fully elucidated with regard to their mechanisms of action. As I said before, if you would like to have me go look at the effects of diisocyanates on glutamatergic neurotransmission, I could do that.

Just everything hasn't been done. I have to

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take the science as I find it and then relate it to my understanding of the mechanisms of action and how the neurodegenerative disease works from what is known and make an opinion. I can't make up science that doesn't exist. I have to follow the science that is there, and I have to follow the logic, and I have to come to a conclusion. The missing data, hopefully, someday will emerge. Maybe it will never be found.

Q. In follow up to that then, if you would look at paragraph 7 of page 2 of the overview of your general causation.

(Witness complying.)

Q. In paragraph 7, you start by saying, "While few studies have looked at age of onset of ALS among subjects exposed to chemicals, many researchers have looked for chemicals that can slow the disease."

A. Right.

Q. What studies are you referring to, if any?

A. If you look at the ALS literature, most studies look at incidence and prevalence of the disease. They don't look at age of onset.

Q. Are there any that look at age of onset that you are aware of?

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A. You know, I would have to go back and look. There is a couple that have included age of onset in their work, but they are very few and far between. There is just not much. I can't recall a specific reference off the top of my head by name. But they just haven't been done as extensively at this point. It has only emerged in the past, I would say, five years has it become en vogue in epidemiology to look at age of onset when you are talking about chemical exposures.

And most of the money right now is looking at Parkinson's disease. ALS does not get as much research funding as Parkinson's disease does, and that impacts on the studies that are done and the amount of studies that are done. Those are just things I can't control.

Q. That is a good segue into my next question. You testified extensively about your Parkinson's-related research. What research have you done with regard to ALS, if any?

A. I have not done any ALS research, per se. I have not been involved in any ALS studies, per se. I have studied ALS in my training. I have been in communication with colleagues to look at, actually,

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some compounds that we have that we are looking at as therapies for ALS. These are compounds that act as allosteric modulators, the NMDA receptors and AMPA receptors, which are glutamate receptors, and we have talked about using these compounds in superoxide dismutase mice to see if we can slow the progression of the disease in them. Those studies have not been initiated yet, but they are studies that we are contemplating doing with possibly collaboration with colleagues that do this work.

Q. Is it generally accepted in the medical and scientific communities that toluene causes ALS?

A. No. Toluene doesn't cause ALS. I don't say that either.

Q. Is it generally accepted in the medical and scientific communities that toluene hastens the onset on ALS?

A. The relationship between toluene and ALS specifically has not been reported.

Q. On page 9, paragraph 6 --

(Witness complying.)

Q. You say -- are you with me?

A. Yes.

Q. Second sentence, "It is my opinion to a reasonable

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degree of certainty --"
Is that scientific or medical, first of all, or both?
A. Both.
Q. "-- that Mr. Allen was genetically predisposed to develop ALS and would likely have seen the course of ALS progress fatally later in life."
What information do you rely upon to arrive at that opinion that he was genetically predisposed? Just the simple fact that he got it?
A. Well, we know that there are familial forms of ALS --
Q. Which he didn't have?
A. -- which he didn't have.
But because we know that there are familial forms of the disease, we know that the disease has a genetic component. We know that the superoxide dismutase is implicated in those genetic forms of the disease. We know in the animal model that the superoxide dismutase mutant mice develop a motor neuron disease.
So we know that, based on our understanding of the disease to this point and it being a disease, that it has to involve some sort of a genetic factor

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for it to be a disease. If is it not, then it is going to be a toxic effect or it is going to be a virus or it is going to be something else.
So if it is a disease and it is happening within an individual and it is not caused by something else, then it has got to be genetic. It has got to be a genetic disregulation that causes the cell to die. There is nothing else. Because something else would not be a disease by definition. It would be a toxic effect, or it would be a viral infection, or it would be something else.
So a disease just is what it is. It is just not a toxic effect. So I use the word "genetics" because defining what a disease is, it is a predisposition. You are born with this genetic predisposition or you are not going to get it. You know, you are --
Q. When you referred to the animal models a moment ago, is it a common pathology that is the same for all the neurodegenerative disease including Parkinson's and ALS, or are there pathologies that --
MR. MAHONEY: Strike that.
Q. Are there common pathologies that are the same for all neurodegenerative disease including Parkinson's

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and ALS, or are there animal models that are closer to a pathology for ALS?
MR. GOTZ: Objection.
A. You use different animal models for different neurodegenerative disease. The animal model for Parkinson's disease is not -- the superoxide dismutase mouse is not what you would use to study Parkinson's disease. You can induce Parkinsonism in mice with different chemicals, and then you can interact those with glutathione S-transferase polymorphisms to actually look at the interaction between oxidative stress and the progression of the disease in the mouse model. In fact, a study just came out showing precisely that, that this interaction occurs there, too.
So when you cannot effectively scavenge free radicals, you actually get a younger and faster progression in the mouse model in Parkinson's disease, too.
Q. So are you relying upon that study to support your opinion that the exposure to toluene hastened the onset of ALS?
A. Actually, the mechanism of action is what I rely on in the ALS model. I am giving an example there.

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But the common mechanism in this case is oxidative stress. In fact, both cases share that. Oxidative stress plays a role in both diseases. So I would expect that when you combine glutathione S-transferase polymorphism with a superoxide dismutation that you would get an animal who developed ALS sooner.
I don't recollect off the top of my head if those studies have been done. But if they have not, I am sure they are ongoing because it is just a really pretty obvious interaction, so.
Q. On page 9, again paragraph 3, you said, "Although numerous solvents and other industrial chemicals have neurotoxic properties, past exposure to these agents is often difficult to quantify and validate, making these studies difficult to design and interpret."
In this case, the exposure to toluene that you believe triggered the early onset of ALS is based upon the symptoms, is that right, not any study that shows a certain level of toluene will hasten the onset of ALS?
A. I'm sorry. Could you rephrase that? So you are basing what I am saying here --

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Q. Yes. In paragraph 3, you say, "Although numerous solvents and other industrial chemicals have neurotoxic properties, past exposure to these agents is often difficult to quantify and validate, making these studies difficult to design and interpret."
Is that fair to say?
A. That is fair to say.
Q. So let me ask the question in another way. How is this case not difficult to design and interpret when we can't quantify the exposure that Mr. Allen had to toluene?
MR. GOTZ: Objection.
A. Well, when you are doing a study like this, say a cohort study, usually a retro cohort study where you look at past history of exposure and you try to quantify the exposure history, you are usually talking a questionnaire. These are studies I have been involved with. You are giving it to someone and you are saying, what was your exposure history and what was this and what was that.
The problem with that is that it is very difficult to get exact exposure histories because you don't have, again, you don't have exposure levels.

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Q. Which we don't in this case; right?
A. But what we do have in this case is the symptoms that he was seen to have by coworkers and others who saw him and that he reported. With a questionnaire where somebody just tells you and nobody else is in the room, you have to rely completely on the patient's own reporting which may have occurred 20 years ago. They may not remember the exact chemical name. You are not going to have material safety data sheets. It becomes even more difficult than it is in in this case. In fact, it is very problematic.
The work I have done in this area -- this is why in science we spend years and years and years trying to arrive at conclusions because we either have to do a prospective study which takes 20 years to complete, or we have to work backwards. And working backwards in a large population is just very, very difficult to do. The epidemiological studies are very, very difficult to do, and they are difficult to interpret.
That is why you cannot interpret science based on epidemiology alone. You have to look at the mechanism of action. You have to look at all

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kinds of things to make that interpretation. Because they are just so problematic. It is very, very -- that is one of the reasons why in my career as a toxicologist I have chosen not to stay in epidemiology. I was asked to go work in the environmental, in the occupational health program at Harvard, and I turned down Harvard to stay at Boston University to go back in the lab, because it is just so difficult.
Q. Isn't your reliance on the reports of Mr. Allen's symptoms anecdotal rather than scientific, reliable evidence such as an indoor air quality test?
A. Unfortunately, that is true.
Q. Paragraph 4 on page 9, I want to ask you what you specifically mean by the phrase "may precipitate ALS."
A. In science -- and I have to qualify this. Specifically in science, we never can say that something causes something. We do studies and we do research and we say this suggests, this indicates, this may be the cause, this may be what happened. We always leave things open ended. We never say this is an absolute truth. It is just how we work as scientists. We gather data, we collect data, and

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we interpret data, and we interpret it in the context of other data.
So when you are looking here and you are saying "environmental toxicity in a susceptible host," they are talking about a situation with a paraoxinase gene with sporadic ALS. Peroxidase is an enzyme involved in the metabolism of many pesticides like corparaphos and parathion. And these genetic predispositions can interact with environmental factors.
In this case, because peroxidase is involved in metabolism of organophosphate compounds which can cause what we call an organophosphate-induced delayed neuropathy, we can start to ask the question of, well, could a genetic mutation like this interact with the environment to actually cause a syndrome virtually identical to ALS? I would again argue -- and this is where you have to interpret everything in context -- that is a toxic effect interacting with a genetic predisposition to cause an increased risk for damage to motor neurons.
But it is not the same as familial ALS, and so this statement is demonstrating how the genetics can interact with the environment to cause a loss of

neurons in a way similar to ALS and gets at how these interactions occur.

So again, this is putting together the pieces of the puzzle. This is where I live and breathe. I have to function within taking somebody else's work and building upon it to make reasonable conclusions. I would never say unequivocally that this causes ALS or may precipitate ALS. That, again, is their work.

And people, you know, are going in that direction, but I think that we always have to be careful in how we think about disease. But it certainly demonstrates, again, this is what is important from the perspective of what is going on here is the ability for this interaction to occur.

Q. Would you agree with me if I said that the evidence of the symptoms that Mr. Allen exhibited after his alleged exposure to toluene is the foundation of your opinion that he did suffer from some exposure to toluene?

A. Say that one more time?

Q. Would you agree with me that the evidence of the symptoms that he exhibited after he was allegedly exposed during the floor refinishing process is the

foundation of your opinion that he was exposed to toluene?

A. That, in combination with the material safety data sheets and the fact that toluene was known to be in the environment. So I have two things. I have the individual and the chemical in same environment, and I have clinical manifestations that can be caused by the chemical, so.

Q. But the material safety data sheets point to specific amounts that are adverse health effects in the environment; is that right?

A. Materials safety data sheets I don't think necessarily do that. The material safety data sheets usually, if they may cause central nervous system problems, they don't usually say a concentration that can cause them.

What they do typically say is the percentage of the chemical that is in the compound. So the 10 percent toluene in that compound is a particularly significant percent of that compound that is toluene.

Now you take that compound, and you spread it all over a gym floor, and you have got a volatile organic compound that vaporizes into the air and

builds up into the air. That is a lot different from a polymer, which is the heavy thing that stays down. Your interactions with toluene, because it vaporizes and can be breathed in pretty easily, you have got a lot of -- even though there is maybe 10 percent, you are spreading this all over a floor, and you can develop pretty significant concentrations in the atmosphere, so.

Q. But we have no --

A. Then you start to see symptoms.

Q. But we have no quantitative evidence of what the levels were?

A. Unfortunately, we don't.

Q. So in relying upon the --

MR. MAHONEY: Strike that.

Q. There are not studies that show -- I just want to make sure we covered this.

There are no studies that show the latency period of ALS; is that right? They just don't exist?

A. No, we wouldn't know. Right. We wouldn't know that somebody had it.

Q. And in the material safety data sheet, is there a warning that says that exposure to toluene may

hasten the exposure to ALS?

A. No.

Q. That is a no?

A. No.

(Recess taken at 4:39 p.m.)

(Recess ended at 4:41 p.m.)

MR. MAHONEY: We are finished.

MR. GOTZ: I have no questions.

(Whereupon, at 4:41 p.m., the deposition was adjourned.)

ATTACH TO DEPOSITION OF: MARCIA H. RATNER, Ph.D.
CASE: LAURA ALLEN, INDIVIDUALLY; And As ADMINISTRATRIX OF THE ESTATE OF DANIEL ALLEN; And AS NEXT FRIEND OF TAYLOR ALLEN AND DANIELLE ALLEN; And MARK ALLEN vs. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES; SOUTHWEST RECREATIONAL INDUSTRIES, INC., d/b/a MARTIN SURFACING

ERRATA SHEET

INSTRUCTIONS: After reading the transcript of your deposition, note any change or correction to your testimony and the reason therefor on this sheet. DO NOT make any marks or notations on the transcript volume itself. Sign and date this errata sheet (before a Notary Public, if required).

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I have read the foregoing transcript of my testimony, and except for any corrections or changes noted above, I hereby subscribe to the transcript as an accurate record of the statements made by me.

MARCIA H. RATNER, Ph.D.

CERTIFICATE

Commonwealth of Massachusetts
Suffolk, ss.

I, Megan McGovern Williams, a Notary Public in and for the Commonwealth of Massachusetts, do hereby certify:

That MARCIA H. RATNER, Ph.D., the witness whose deposition is hereinbefore set forth, was duly sworn by me and that such deposition is a true record of the testimony given by the said witness.

IN WITNESS WHEREOF, I have hereunto set my hand this day of , 2007.

Megan McGovern Williams
Shorthand Reporter

My Commission expires:
August 23, 2013

EXHIBIT F

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN Plaintiffs	CIVIL ACTION NO. 05-40048-FDS
v.	
MARTIN SURFACING, A DIVISION OF SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC., d/b/a MARTIN SURFACING; Defendants	

RULE 26 EXPERT REPORT – WILLIAM M. EWING, CIH

At the request of Mr. Mike Hugo and Ian McCallister of Brent Coon & Associates I was asked to review information concerning the resurfacing of the gymnasium in the Field House at Holy Cross to prepare opinions regarding exposures to Coach Dan Allen resulting from this work and related industrial hygiene issues. Industrial hygiene is the field devoted to the identification, evaluation and control of health hazards in the workplace.

I am the Technical Director for Compass Environmental, Inc. located at 1751 McCollum Parkway, Kennesaw, GA 30144-5908. Compass Environmental, Inc. is an industrial hygiene consulting firm that conducts industrial hygiene studies for governmental entities and private companies. Compass also conducts training and research in areas related to industrial hygiene. As Technical Director my responsibilities include preparation of industrial hygiene study designs, conducting field work, preparation of reports and training materials, quality control, and review of other industrial hygienists' work.

My formal education consists of a BS degree in biology from Washington & Lee University (1978) with additional course work in statistics, and technology & science policy at the University of Michigan, Georgia State University, and the Georgia Institute of Technology. I have also completed classes in industrial hygiene, toxicology, respiratory protection, asbestos control, environmental assessments, indoor air quality, and related subjects.

I am certified in the comprehensive practice of industrial hygiene by the American Board of Industrial Hygiene (No. CP 2627). This certification required I complete the core certification examination following at least one year full-time industrial hygiene experience, and the comprehensive practice examination after 5 years of full-time industrial hygiene experience. I passed my core examination in 1980 and my comprehensive practice in 1983. I have maintained my certification since that time and in 2007 my certification was extended until 2012. In 1993 I passed the sub-specialty examination in Indoor Environmental Quality.

I am a member of the American Industrial Hygiene Association (AIHA), the American Conference of Governmental Industrial Hygienists (ACGIH), the National Institute of Building Sciences (NIBS), the American Society for Testing and Materials (ASTM), the International Society of Indoor Air Quality and Climate (ISIAQ), and several other professional or technical organizations. I serve on the AIHA Indoor Environmental Quality Committee and previously was chairman of this committee. I am a member of the AIHA Practices, Standards and Guidelines Committee and served as its chair in 2004. I was recognized as a Fellow Member in 1995 by the AIHA.

I have practiced industrial hygiene for 29 years. Most of my work has focused on the identification, evaluation and control of airborne contaminants. This includes anticipating the release of contaminants during various work activities, determining pathways of exposure, measuring exposures to workers and bystanders, and controlling exposures following the hierarchy of controls concept. As an industrial hygienist I am knowledgeable of general and local exhaust ventilation principles, design and operation. I am familiar with the regulations affecting workers' exposures to chemicals promulgated by the Occupational Safety and Health Administration (OSHA). I am also familiar with recommended practices and guidelines put forth by the National Institute for Occupational Safety and Health (NIOSH), the ACGIH, and other organizations. My CV is attached providing additional information, including a list of my publications. Also attached is a list of my trial and deposition testimony covering the last 5 years. Compass Environmental, Inc. invoices $185 per hour for my time.

To gain an understanding of the facts surrounding the floor resurfacing I was provided the following materials to review.

Affidavit of Paul Crecelius
Affidavit of Paul Bachia
Affidavit of Robert Bradley
Video taken on May 14, 2007 during a visit to the Holy Cross field house
Scott Merrill deposition taken June 14, 2007
Rod Paul deposition taken April 11, 2007
Technician's Manual for the Installation of Versaturf "360" manufactured by Martin Surfacing, Inc.
Technical data, diagrams, and parts lists for Graco, Inc. airless sprayers

Lord Chemical Products, "Troubleshooting & Application Guidelines for Chemglaze Coatings for Synthetic Athletic Floors."
Martin Surfacing, Inc., "Versaturf 360 Monolithic Floor System Specification"
Dan Allen, Personal Medical History (4 pages)
Laura Allen answer to Interrogatory No. 2 (1 page)
Material Safety Data Sheets for Martin Surfacing, Inc. (Bates Nos. HC01532-746)
Additional Material Safety Data Sheets
NOAA Local Climatological Data, Worcester, MA for May and June 2001
Martin Surfacing Pre-Installation Checklist, and other miscellaneous documents with Bates Nos. HCO 1436-1445
Resurfacing Specifications for Urethane Flooring (Bates No. 000179-181)
Martin Surfacing product information for Versaturf 360 (Bates Nos. 000218-220)
Floor (piping) plans (M-1 and M-2) for the Holy Cross field house (2 pages)
Mechanical plans (M-3 and M-4) for the Holy Cross field house (2 pages)
Rule 26 Expert Report of Marcia Ratner, Ph.D. dated June 14, 2007

From my review of these materials it is my understanding that Holy Cross contracted with Martin Surfacing, Inc. (owned by Southwest Recreational Industries, Inc.) to remove the worn infield athletic surface from the field house gymnasium and install a new Versaturf 360 surface. The work apparently occurred over a one to two week period in late May and/or early June 2001. The area to be resurfaced was stated to be 17,000 square feet on the first floor.[1] At any given time there appears to have been no fewer than two, nor more than five contractor employees at the site performing the work. According to Mr. Paul Crecelious, the floor surface was prepared by sanding and then vacuuming to remove loose debris and dust. A primer was then spray applied to the floor surface. After allowing time to dry (probably overnight) the two part polyurethane liquid floor surface material was poured onto the floor and raked out to provide a single seamless membrane when it cured. One or more coatings were then applied to the floor.[2] The final floor, based on the site visit conducted in 2007, was tan in color with white and red lines for the basketball courts. According to Mr. Paul's testimony and Mr. Crecelious' affidavit the workers wore full-face negative pressure air-purifying respirators during the spray operations. To what extent partial or full body protective clothing was worn is unclear. The final steps appear to have been to apply small amounts of primer for the lines and then painting the lines. This final work was done using hand rollers.

The field house was reported originally constructed for the military and physically moved to the Holy Cross campus in the middle of the last century. The total foot print of the building is approximately 25,000 square feet. Most of the first floor is taken up by the gymnasium. A lobby, office area and weight room comprise the remainder of the first level. There are two suites of offices on the second floor comprising about 10,000 square feet. Coach Dan Allen's office was room 214 depicted on drawing M-2. [Note: the rooms have since been renumbered.] One air handling unit was present (and remains) suspended above the gymnasium floor in the northwest corner. This unit is rated at 9705 cubic feet

[1] Deposition of Rod Paul, April 11, 2007, p. 81.
[2] Witness recollections and generic specifications do not agree on how many and exactly which coatings were applied on the Holy Cross job.

per minute (CFM). This is the amount of air it moves to the three office areas it serves on the first and second floors of the field house. The design specifications called for a supply volume to Coach Allen's office of 380 CFM and a return volume of the same amount. The design specifications for the system provided for 2790 CFM to and from the first floor offices. The damper setters per the design would allow for a minimum amount of outside air to be 2275 CFM and a maximum of 9705 CFM. Based on my experience the damper setting was most likely set at 25-50% outside air as an energy conservation measure. The system was designed to be able to both heat or cool the air provided to the office spaces. All return air from all office spaces went to a central mixing box where it was mixed with some outside air, passed through a filter to remove coarse particles, then heated (or cooled), and delivered back to the office spaces through the supply air ducts and diffusers mounted in the ceiling. The air handling unit was apparently operating when the floor resurfacing work occurred. It has not been determined if the system shut down in the evenings.

The open gymnasium area on the first floor relies on natural ventilation. There are approximately 4 or 5 roof-mounted exhaust units that according to Mr. Scott Merrill are equipped with fans. There are three additional exhaust fans in the weight rooms that are designed to pull 11,377 CFM from the gymnasium space into the weight rooms and back into the gymnasium space. It is not clear if any of these exhaust fans were operating during any time the floor was being resurfaced. During the work on the gymnasium floor witnesses reported conflicting accounts on whether exterior (and interior) doors were opened or closed. It appears quite likely that at some times they were opened and at other times closed depending on the work activity, temperature, and need to control the relative humidity during the curing process of the polyurethane. According to various Martin surfacing specifications and the installation manual, the relative humidity should have been maintained below a value of 50 – 68% for a proper cure and prevent a tacky surface. Mr. Paul Crecelious also reported that at some point in the process (after the floor was dry) an industrial exhaust fan was placed in an exterior door to blow the fumes out.

It is not possible to predict with any degree of accuracy the amount of air that moved from the gymnasium to the upper office area where Coach Allen was located based solely on the ventilation design for the building and the conflicting recollections of the witnesses. It is clear that significant concentrations of volatile organic vapors (VOCs) did migrate to Coach Allen's office and other offices on his corridor based on the symptoms experienced by Mr. Allen and his co-workers. The specific symptoms of headache, dizziness, and nausea demonstrate concentrations likely to be well in excess of documented order threshold values reported by the AIHA.[3] Reviewing the Material Safety Data Sheets (MSDS) for the chemicals used during the floor resurfacing, the VOCs would have been in the form of mixtures. This is addressed further below.

[3] American Industrial Hygiene Association (AIHA), *Odor Thresholds for Chemical with Established Occupational Health Standards*, AIHA, Fairfax, VA (1989).

Floor Preparation and Primer

It is not expected the preparation phase of the work that included sanding of the old floor surface would have generated significant VOCs. Some amount of dust would have been generated, however no witnesses indicated that dust was a problem. Once the floor was vacuumed the primer would have been applied. Based on the Martin Surfacing Installation Manual the Martin 2164 Urethane Primer would have been applied undiluted at a rate of 700 square feet per gallon. This material would have been applied with an airless sprayer. According to the MSDS submitted to Holy Cross, the Martin 2164 Urethane Primer contained the following volatile components.[4]

Chemical	Wt. % Less Than	CAS Number
Ethyl benzene	10	100-41-4
Xylene	35	1330-20-7
Methyl Ethyl Ketone (MEK)	45	78-93-3
Toluene	10	108-88-3

Section 9 of the MSDS states the volatile components by weight comprise 89.6% of the primer and section 16 states the volatile organic components comprise 6.45 pounds per gallon. Assuming the workers applied the primer as specified (700 ft^2 per gallon), then 24.3 gallons of primer was used. This would result in the application and subsequent release into the air through evaporation of 24.3 gallons X 6.45 pounds per gallon = 156.7 pounds of volatile components. Using the above percentages, the amount of each volatile component should have been as follows:

Chemical	Lbs.
Ethyl benzene	15.7
Xylene	54.8
Methyl Ethyl Ketone (MEK)	70.5
Toluene	15.7

Polyurethane Floor Membrane

Once this material was allowed to dry (all volatiles organics evaporated) the pouring of the polyurethane floor membrane could occur. According to the materials reviewed, this likely occurred during one day. The polyurethane floor application was performed by metering out the two components of the Versaturf 360 liquid floor surfacing. These two parts are Part A, the resin, and Part B, the hardener. Part A consisted of polyoxy propylene glycol (65%) along with fillers (silica, clays) and iron oxide for color (35%). Part B consisted of a blend of diisocyanates. The machine would pull each part from separate drums and dispense the product into five gallon buckets. The workers would pour the liquid onto the floor and rake it into place forming a seamless floor membrane.

[4] Martin Surfacing, Inc., Material Safety Data Sheet for 2164 Urethane Primer, 2/20/94, Bates Nos. HC01592-96. Note page 1 of the MSDS is missing, constituents derived from section 15 on page 6.

These materials are designed to react to form the urethane polymer comprising the floor as it cures. The components of these chemicals are not very volatile. Apparently the workers performing this work did not wear respiratory protection. Considering the low Threshold Limit Value (TLV) for the diisocyanates this was probably not prudent, however, it is unlikely there was any significant concentration in areas outside the gymnasium proper. Furthermore, the concentration of diisocyanates in the gymnasium was likely quite low as well.

Primer for Urethane Coating

Once the urethane membrane had set (but not completely cured) the primer could be applied prior to the top coat. The material called for in the installation manual, and matching the MSDS submitted to Holy Cross was the Martin A.P. Concentrate. This material was mixed at a rate of 1 part A.P. Concentrate to 4 parts solvent. The solvent, referred to as Martin Blend, consisted of a 50/50 mix of xylene and cellosolve acetate (also known as 2-ethoxyethyl acetate). According to the installation manual the application rate for this primer is 400-800 ft^2 per gallon. Accordingly it would have required 21-43 gallons of the mixed primer to cover the 17,000 ft^2. This corresponds to 4-9 batches of five gallons each. Based on the constituents listed, considered volatile, listed below are the range of quantities of VOCs that would have been emitted during this phase of the floor resurfacing work.[5] The weight percent reported in the MSDS was used with the weight of VOCs per gallon reported in section 16 of the MSDS of 3.82 lbs/gal to complete the following table.

Chemical	Min. (gal.)	Max(gal.)	Lbs. (Min.-Max)
Xylenes (in solvent & concentrate)	8.8	19.8	33.6 – 75.6
Cellosolve acetate	8.0	18.0	30.6 – 68.8
Toluene	0.8	1.8	3.1 – 6.9
Ethyl benzene	0.16	0.36	0.6 – 1.4
Methyl isobutyl ketone (MIBK)	0.16	0.36	0.6 – 1.4
1-methoxy-2-propyl acetate	0.12	0.27	0.5 – 1.0

Apparently during the spray application of this primer the floor surfacing workers wore full-face negative pressure air-purifying respirators equipped with organic vapor cartridges.[6]

Urethane Coating

After allowing the primer to dry, a urethane coating was applied over the new floor. Based on the final floor color (tan) and the submittal to Holy Cross, the coating was likely Martin Surfacing, Inc. S2951 Tan Flat urethane coating. The application rate was

[5] Note: Calculation is based on the percentages reported in the MSDS for A.P. Concentrate. Toluene-2,4-diisocyanate (TDI) present in the concentrate at 1% was not included as it would not be considered volatile to the extent that it might present a significant exposure to persons outside the gymnasium.
[6] Rod Paul deposition of April 11, 2007, p. 26.

likely 125 ft^2 per gallon.[7] For the 17,000 ft^2 floor surface this would have required 136 gallons of tan urethane coating. The percent volatile (by weight) for this compound is stated as 63.3% and the percent volatile by volume as 72.8%.[8] Based on the constituents listed in the MSDS it appears these are reversed and the actual percent volatile by weight is 72.8%. Based on the application rate the quantity of VOCs released during this process should be as follows. The weight of VOCs in the table below is based on the MSDS VOC concentration of 5.43 lbs/gal reported in the MSDS using the 136 gallons applied using the calculation 139 lbs. X 5.43 lbs/gal X weight percent of each component.

Chemical	Gal.	Lbs.	CAS Number
Ethyl benzene	6.8	36.9	100-41-4
Methyl isobutyl ketone	13.6	73.8	108-10-1
1-Methoxy-2-propyl acetate	34.0	184.5	108-65-6
Toluene	13.6	73.8	108-88-3
Xylene	27.2	147.6	1330-20-7
Dipropyleneglycol methyletheracetate	5.4	29.5	88917-22-0

In the above list I did not include the titanium dioxide (opacity filler) or the unspecified coloring agent as these would not be volatile. I also did not include the two isocyanates or the catalyst assuming they would have reacted completely in the mixture. Again, the floor coating workers would have wore the full-face negative pressure air-purifying respirators during the application of the urethane coating with the airless sprayer. This process should have occurred during a single shift and likely allowed to dry overnight.

Game Line Application

The last step in the floor surfacing would have been to measure and tape the game lines. Once the tape was down, a game line paint primer (Martin Surfacing, Inc. Primer 2169) would have been applied with a roller.[9] Once the primer dried (at least 4 hours, or more likely overnight) the game lines were painted using a roller. The white lines were probably painted using Martin Surfacing, Inc. S2107 White Coating.[10] The red lines were likely either Martin Surfacing, Inc. Aviation Red/Flat or Track Brick/Red Flat coating.[11] While each of these primers and paints contain VOCs the actual amount of coverage in square feet would have been small, with relatively small releases of VOCs.

[7] Martin Surfacing Installation Manual at page 33 describes mixing and spraying the urethane coatings. This manual allows for three different procedures. The procedures all would result in similar releases of the same VOCs during application, although the 25 gallon batch process would result in some additional forms of VOCs from the solvent used.
[8] Martin Surfacing, Inc., Material Safety Data Sheet, S2951 Tan Flat, Bates Nos. HC01619-24.
[9] Martin Surfacing, Inc. Installation Manual, p. 36.
[10] Martin Surfacing, Inc., Material Safety Data Sheet, S2107 White Coating, Bates No. HC01713-19.
[11] Martin Surfacing, Inc. Material Safety Data Sheets (3) at Bates Nos. HC01669-92.

Other Solvents

I also recognize that additional quantities of solvents were used by Martin Surfacing, Inc. employees to clean and flush the application equipment. Which solvents were used, in what quantities, and what was done with the solvent waste has not yet been determined.

Based on this understanding of the activities that occurred during the floor resurfacing in the field house there was likely three separate days when major releases of VOCs occurred. These were the two primer applications and the urethane coating application. There were at least three pathways of exposure to the upper offices where the symptoms were expressed by Coach Allen and his co-workers. One pathway was via the first floor offices that would return air to the air handler mixing box and redistribute that air to the three office areas. The second would be through leakage into the return air duct and points upstream of the air handling unit fan located in the gymnasium proper. The third pathway would be through simple migration from space-to-space.

The symptoms of headaches, dizziness and nausea are classic for overexposure to xylenes, toluene, methyl ethyl ketone, ethyl benzene, and methyl isobutyl ketone. The amounts released into the air of the building were not trace amounts, but hundreds of gallons representing hundreds of pounds of these compounds. Likewise, the symptoms associated with excessive exposure to acetates, such as the cellosolve acetate, according to the OSHA data sheet for this compound include headaches, dizziness, and nausea.[12] It is likely the reported symptoms were from exposures to the combination of VOCs in about the same ratios as used during the floor installation.

Ambient Climatological Data

During the preparation of this report I reviewed the climatological data for May and June 2001. Summarized below are the findings for temperature and percent relative humidity during the last ten day of May and the first ten days of June.

Ambient Temperature and Relative Humidity for Worcester, MA during May 22 – June 10, 2001[13]

Date	Temperature (F)			Average Wet Bulb (F)	Relative Humidity (%)	Comments
	High (F)	Low (F)	Average (F)			
5/22	52	48	50	50	100	Rain, Heavy Fog, Mist
5/23	57	47	52	46	65	Rain, Heavy Fog, Haze
5/24	62	47	55	46	50	Rain, Mist, Haze
5/25	64	46	55	49	67	Rain
5/26	68	48	58	53	72	Rain, Mist

[12] Occupational Safety and Health Administration (OSHA), Data Sheet for 2-Butoxyethyl acetate (available at www.osha.gov).
[13] National Oceanographic & Atmospheric Administration (NOAA) National Climatic Data Center, Worcester Regional Airport Station.

5/27	58	54	56	N.D.	N.D.	Rain, Heavy Fog, Mist
5/28	69	51	60	N.D.	N.D.	Rain, Mist
5/29	67	49	58	53	72	Rain
5/30	57	42	50	44	64	Rain
5/31	61	39	50	44	64	
6/1	69	43	56	48	58	
6/2	65	51	58	N.D.	N.D.	Rain, Heavy Fog, Mist, Haze
6/3	64	51	58	N.D.	N.D.	Rain, Heavy Fog, Mist, Haze
6/4	64	50	57	53	77	
6/5	69	50	60	55	72	
6/6	71	54	63	55	61	
6/7	74	53	64	46	22	
6/8	76	56	66	54	46	
6/9	76	59	68	55	43	
6/10	79	58	69	57	48	

N.D. = No data

Good industrial hygiene practices call for the identification, evaluation and control of health hazards in the workplace. The application of polyurethane floor surfaces provides numerous opportunities for workers' exposure to various organic compounds (specific ones described above) and to the diisocyanates. Martin Surfacing, Inc. was required under the OSHA regulations to conduct air sampling during this project, unless they had accumulated a large quantity of data from many other substantially similar projects. The purpose for this sampling is to determine if the personal protective equipment (e.g., respirators) provided to workers is providing adequate protection. It is odd that the MSDS for these products state that if you spill the product, a self-contained breathing apparatus (SCBA) should be used for clean-up. However, here the workers were intentionally spraying the products (hundreds of gallons) onto the floor while wearing only full-face negative pressure air-purifying respirators. At the time, SCBA was rated with a protection factor of 10,000 and the full-face air-purifying respirator was rated at 50. This means the SCBA should reduce the exposure by a factor of 10,000 while the other by a factor of 50, if properly fit-tested and used by properly trained workers.

When conducting sampling the results are generally compared against the OSHA permissible exposure limits (PELs), the ACGIH Threshold Limit Values (TLV), or other guidelines. It should be noted that when there are exposures to multiple exposures to different chemicals that have effects on the same target organs or systems the industrial hygienist considers the exposure to the entire mixture. This is explained by the ACGIH as follows:

When two or more hazardous substances have a similar effect on the same target organ or system, their combined effect, rather than that of either individually, should be given primary consideration. In the absence of information to the contrary, different substances should be considered as additive where the health effect and target organ or system is the same. That is, if the sum of

$$C_1/T_1 + C_2/T_2 + \ldots C_n/T_n$$

exceeds unity (one), the threshold limit of the mixture should be considered as being exceeded (where C_1 indicates the observed atmospheric concentration and T_1 is the corresponding threshold limit.)[14]

Another reason for conducting air sampling is to determine what exposures may result to bystanders by the floor surfacing work. In a multiemployer worksite, such as the field house when the floor was being resurfaced, the responsibility for worker health and safety is different than when only one employer is present at a worksite. An employer that creates a hazard by their activities has responsibility for their own employees as well as others that might be affected by the hazard. Employers also carry responsibility for the health and safety of their own employees. Lastly, the workers themselves are responsible to use the protective equipment they have been provided (and trained to use), and follow the work practices they have been trained to use.

I have requested any air sampling data that might have been collected during the floor resurfacing project at the field house in 2001. I have also requested any air sampling data from other jobs that Martin Surfacing, Inc. performed while installing polyurethane floor surfacing. I understand none were taken at the Holy Cross field house project.[15] I have not seen any from any other Martin Surfacing, Inc. projects and do not know if any exist. Without air sampling data it is difficult for an employer to evaluate the extent of the hazard posed to workers and how to control those hazards.

To control a hazard industrial hygienists rely upon a concept know as the hierarchy of controls. The first choice is to eliminate the hazard through substitution. This could include the elimination of a hazardous material, or selection of a less hazardous substance, if feasible. For example, Martin Surfacing, Inc. MSDS sheets for some of their paints used on athletic surfaces contained high concentrations of lead. They should not have still been using lead and lead chromate paints. Martin Surfacing, Inc. should have investigated using substitute solvents and a substitute for the isocyanates. I do not know whether they did this at some point or not.

If a hazard cannot be eliminated through substitution, every effort should be made to engineer out the hazard. The use of engineering controls greatly reduces the chance of human error. Segregation of the work, enclosures, and local exhaust ventilation are typical examples.

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[14] ACGIH, *2006 TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices,* ACGIH, Cincinnati, OH (2006), p. 85

[15] Note: I understand some air sampling was conducted approximately 15 months later in the field house. It is unlikely these results, should they become available, will be helpful in retrospectively establishing exposures from May — June 2001.

Work practices designed to reduce exposures should always be used where feasible. For example, a paint roller can be used to apply the primer instead of an airless sprayer. Administrative controls can also be used. For example, the work resulting in possible exposures to bystanders can be done when those persons are not present (after hours).

The last choice in the hierarchy of controls is to put workers in respirators. The respirator becomes the last line of defense for an inhalation hazard. For a tight-fitting full-face air-purifying respirator, such as that worn by some workers at the field house project, to be effective, it must be properly fitted and the workers enrolled in a respiratory protection program. The workers must be trained and understand that facial hair, or even a couple of days without shaving, can compromise the seal between the mask and the face greatly reducing the effectiveness of the device.

One of the most important elements of an effective industrial hygiene program is education of the worker. The workers need to know the extent of hazards associated with their work and how to protect themselves. This is usually done through an effective hazard communication program as described in the OSHA standard at 29 CFR 1910.1200. If workers need to wear respirators, they also need training in respiratory protection as described at 29 CFR 1910.134. Workers wearing a respirator must first have a medical determination to be certain they are capable of wearing a negative pressure device without impairing their health.

According to Mr. Rod Paul, Martin Surfacing, Inc. never did worker training.[16] The standard practice appears to have been to have two Martin Surfacing, Inc. employees go to a job site and hire local laborers on a temporary basis to perform much of the work.

As part of my review I searched the on-line OSHA site inspection database for previous OSHA inspection results at Martin Surfacing (or Southwest Recreational Industries) projects. In 1992, Martin Surfacing, Inc. was cited for violations to the OSHA standards regarding personal protective equipment, particularly eye and face protection. In a separate inspection at the same job location they were cited for violating the hazard communication standard. At another project they received three serious citations for violating the hazard communication standard, material safety data sheets, and respiratory protection. In another project in Alexandria, VA they were cited for failure to perform chemical monitoring. These all occurred prior to the Holy Cross project. In August 2002 Southwest Recreational Industries, Inc. was issued nine citations including violations of the hazard communication standard, material safety data sheet violations, personal protective equipment violation, respiratory protection standard violations, medical records access violation, and the failure to provide employee information and training, among others.

In summary, it is my opinion to a reasonable degree of scientific certainty that Coach Dan Allen and some of his co-workers present in the field house during the gymnasium floor resurfacing were exposed to significant concentrations of solvent vapors during at least three days of the work. Based on the information reviewed to date, it is not possible for

[16] Rod Paul deposition of April 11, 2007, p.10.

me to conclude whether Mr. Allen's exposure to any particular chemical was in excess of the PEL or TLV. However, it is likely that Mr. Allen's exposure to this mixture of solvents known to act on the central nervous system approached or exceeded the PEL and TLV for the mixture.

William M. Ewing

William M. Ewing, CIH

June 21, 2007

Date

EXHIBIT G

CURRICULUM VITAE
Marcia Hillary Ratner, Ph.D.

Business Address

Department of Pharmacology and Experimental Therapeutics
Boston University School of Medicine
715 Albany Street, L-603
Boston, Massachusetts 02118-2526
Telephone: 617 638 4440
Fax: 617 638 4329
Electronic mail: marcia@bu.edu

Education and Degrees

Undergraduate

1995	Boston University College of Liberal Arts Bachelor of Arts in Psychology

Graduate

May 2004	Doctor of Philosophy Behavioral Neurosciences Program Boston University School of Medicine

Post Doctoral

2004-present	Post-Doctoral Fellowship Laboratory of Molecular Neurobiology Department of Pharmacology and Experimental Therapeutics Boston University School of Medicine (Mentor: David H. Farb, PhD)

ACADEMIC APPOINTMENTS

1998-present	Research Associate Department of Neurology Boston University School of Medicine (Chairman: Robert G. Feldman, MD)
2004-present	Lecturer Occupational Health Program Department of Environmental Health Harvard School of Public Health

PROFESSIONAL EXPERIENCE

Teaching

2000	Seminar Lecturer Integrated Clinical Problems

Topic: *n*-Hexane Neurotoxicity
Environmental and Occupational Neurology Program
Department of Neurology
Boston University School of Medicine
(Course Coordinator: Allen Geller, Ph.D)

2000-present Instructor
Course Title: Toxicology
Program in Biomedical Laboratory and Clinical Sciences
Department of Biochemistry
Boston University School of Medicine and Metropolitan College
(Program Director: Connie Phillips, MA, MPH)

2001- present Instructor
Course Title: Forensic Toxicology
Program in Biomedical Laboratory and Clinical Sciences
Department of Biochemistry
Boston University School of Medicine and Metropolitan College
(Program Director: Connie Phillips, MA, MPH)

2002 Guest Lecturer in Neurotoxicology
Course Title: Introductory Toxicology
Department of Environmental Health
Boston University School of Public Health
(Course Director: Wendy Heiger-Bernays, PhD)

2003- present Lecturer in Forensic Neurotoxicology
Course Title: Forensic Neuropsychology
Behavioral Neurosciences Program
Boston University School of Medicine
(Course Directors: Paul Spiers, PhD)

2004 Guest Lecturer in Neurotoxicology
Course Title: Neuroscience Biology of Disease Course
Boston University School of Medicine
(Course Director: Thomas Brown, MD)

2004-present Robert G. Feldman Memorial Lecturer in Occupational Neurological Disorders and Neurotoxicology
Course Title: Introduction to Occupational and Environmental Medicine
Occupational Health Program
Department of Environmental Health
Harvard School of Public Health
(Course Director: David Christiani, MD)

2005 Invited CME Lecturer
Massachusetts Neuropsychological Society
Title of Presentation: "Exciting New Frontiers in Neuropsychology: Magnetic Resonance Spectroscopy: The Case for Lead Exposure" Spaulding Rehabilitation

HC02208

Hospital, Boston, MA, February 1st, 2005.

Research

1995-1996	Research Assistant Environmental and Occupational Neurology Program Department of Neurology Boston University School of Medicine (Program Director: Robert G. Feldman, M.D.)
1996-1998	Editorial Research Assistant Publication: "*Occupational and Environmental Neurotoxicology*" Author: Robert G. Feldman, M.D. Publisher: Lippincott-Raven, 1999 Environmental and Occupational Neurology Program Department of Neurology Boston University School of Medicine
1998-2004	Senior Toxicologist and Project Manager Environmental and Occupational Neurology Program Department of Neurology Boston University School of Medicine (Principal Investigator: Robert G. Feldman, M.D.)
2002-2004	Project Manager Gene-Metal Interactions and Parkinson's Disease Sponsor NIEHS Principal Investigators: Howard Hu, MD, ScD, MPH and Robert G. Feldman, MD
2004-	Research Associate and Project Manager Laboratory of Molecular Neurobiology Department of Pharmacology and Experimental Therapeutics Boston University School of Medicine (Chairman and Principal Investigator: David H. Farb, PhD)

Clinical

1998-2005	Senior Toxicologist Environmental and Occupational Neurology Program Department of Neurology Boston University School of Medicine Boston, MA

Business

2002-2004	Vice President and CEO Chemical Safety Net. Inc. Boston, MA and Delaware, MD

HC02209

HC02209

PROFESSIONAL AWARDS AND HONORS

2000-present	Who's Who of American Women
2002-present	Who's Who in America
2002-present	Who's Who in Science and Engineering

PROFESSIONAL ORGANIZATIONS

1998-	Massachusetts Neuropsychological Society
1999-	American Academy of Clinical Toxicology
1999-	International Neurotoxicology Association
1999-	Society for Neuroscience
2000-2004	Society for Occupational and Environmental Health
2001-	American Conference of Governmental Industrial Hygienists
2001-	New York Academy of Sciences

PRESENTATIONS

1. **Ratner M,** Cabello, D, Thaler D, and Feldman R: Movement Disorder in an Adult Following Exposure to DEET. Presented at the North American Congress of Clinical Toxicology, Montreal, Quebec, Canada, October 6, 2001.

PUBLICATIONS

Book Chapters and Peer-Reviewed Articles

1. Feldman RG, **Ratner MH,** and Ptak T: Chronic toxic encephalopathy in a painter exposed to mixed solvents. Harvard School of Public Health, Grand Rounds in Environmental Medicine. Environ Health Perspect, 107(5): 417-422, 1999.
2. Feldman RG, **Ratner MH**, and Feldman ES: Approach to neurotoxicity tort cases. Neurologic Clinics: Medical-Legal Issues Facing Neurologists. Vol 17 (2):267-281, 1999.
3. Feldman RG, and **Ratner MH**: The pathogenesis of neurodegenerative disease: neurotoxic mechanisms of action and genetics. Current Opinion in Neurology, 12:725-731, 1999.
4. Feldman RG, and **Ratner MH**: Essentials of Metal Neurotoxicity: Mechanisms and Pathology. Clinics in Occupational and Environmental Medicine: Neurotoxicology. 1(3):1526-1546, 2001.
5. **Ratner MH**, Feldman RG, and White RF: Neurobehavioral Toxicology. In: Ramachandran V.S. (Ed); Encyclopedia of the Human Brain. New York, Elsevier Science, Vol. 3, pp 423-439, 2002.
6. Feldman RG, and **Ratner MH**: Behavioral Syndromes in Neurotoxicology. In: Fogel BS, Schiffer RB, and Rao SM (eds): Neuropsychiatry. 2nd Edition. Philadelphia, Lippincott-Williams and Wilkins, pp1168-1190, 2003.
7. Feldman RG, and **Ratner MH**: Treatment of Neurotoxic Effects of Gases: Carbon Monoxide, Hydrogen Sulfide, and the Nitrogen Oxides. In: Noseworthy, J. (ed); Neurological Therapeutics: Principles and Practices. London, Martin Dunitz, pp 1526-1530, 2003.
8. Feldman RG, and **Ratner MH**: Heavy Metal Poisoning. In: Lynn, D. J., Newton,†H.B., and Rae-Grant,†A.D. (eds): The 5-Minute Neurology Consult. Philadelphia, Lippincott, Williams & Wilkins, pp 218-219, 2004.

9. **Ratner MH**, and Feldman, RG: Environmental Toxins and Parkinson's Disease. In: Pfeiffer, R.F., and Ebadi M. (eds): Parkinson's Disease. Boca Raton, CRC Press, Chapter 6, pp 51-62, 2005.
10. Feldman RG, Janulewicz PA, and **Ratner MH**: Toxic encephalopathy. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 189-194, 2005.
11. Feldman RG, and **Ratner MH**: Peripheral neuropathy. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 388-394, 2005
12. Feldman RG, and **Ratner MH**: Tremor. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 488-491, 2005.
13. Feldman RG, Janulewicz PA, and **Ratner MH**: Memory impairment. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 332-335, 2005.
14. Feldman RG, Janulewicz PA, and **Ratner MH**: Parkinsonism. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 376-382, 2005.
15. Feldman RG, Nelson S, and **Ratner MH**: Multiple Sclerosis. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 361-365, 2005.
16. Feldman RG, Nelson S, and **Ratner MH**: Smell and Taste Disorders. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 454-457, 2005.
17. **Ratner MH** and Jabre J: Treatment of Neurotoxic Effects of Gases: Carbon Monoxide, Hydrogen Sulfide, and the Nitrogen Oxides. In: Noseworthy, J. (ed); Neurological Therapeutics: Principles and Practices. London, Martin Dunitz, (In Press).
18. **Ratner MH** and Jabre J: Treatment of Neurotoxic Effects of Organic Solvents. In: Noseworthy, J. (ed); Neurological Therapeutics: Principles and Practices. London, Martin Dunitz, (In Press)

Abstracts

1. **Ratner M,** Cabello, D, Thaler D, and Feldman R: Movement disorder in an adult following exposure to DEET. J Toxicol Clin Toxicol, 39: 477, 2001.

Exhibit H

CURRICULUM VITAE

DATE PREPARED: June 15, 2007

Part I:

DEMOGRAPHIC INFORMATION:

Name:	L. Christine Oliver
Address:	1101 Beacon Street Four West Brookline, MA 02446
Place of Birth:	Raleigh, North Carolina

EDUCATION and TRAINING:

Education:

1966	AB	University of North Carolina, Chapel Hill, NC
1970	MD	University of North Carolina School of Medicine, Chapel Hill, NC
1978	MPH	Harvard School of Public Health, Boston, MA
1979	MS	Harvard School of Public Health, Boston, MA

Postdoctoral Training:

1970-1971	Internal Medicine North Carolina Memorial Hospital, Chapel Hill, NC
1972-1974	Social Medicine/Internal Medicine Montefiore Hospital, Bronx, NY
1977-1979	Occupational Medicine Harvard School of Public Health, Boston, MA

Licensure and Certification:

1970	North Carolina License, Medicine, Certificate #03484
1974	New York License, Medicine, Certificate #119861
1975	Massachusetts License, Medicine, Certificate #38968
1974	American Board of Internal Medicine, Certification
1982	American Board of Preventive Medicine, Certification
1980	National Institute of Occupational Safety and Health (NIOSH) "B" Reader Certification Occupational Pneumoconioses
1985, 1989, 1993, 1997, 2001	NIOSH "B" Reader Recertification

PROFESSIONAL APPOINTMENTS:

Academic Appointments:

1974-1975	Assistant Professor of Medicine, Albert Einstein School of Medicine, Bronx, NY
1976-1979	Instructor in Medicine, Harvard Medical School, Boston, MA
1980-1982	Clinical Instructor in Medicine, Harvard Medical School
1982-1986	Instructor in Medicine, Harvard Medical School
1986-1998	Assistant Professor of Medicine, Harvard Medical School
1998-	Assistant Clinical Professor of Medicine, Harvard Medical School

Hospital Appointments:

1974-1975	Assistant Attending in Medicine, Montefiore Hospital, Bronx, NY
1975-1977	Clinical Associate in Medicine, Massachusetts General Hospital, Boston, MA
1977-1978, 1980-1986	Assistant in Medicine, Massachusetts General Hospital, Boston, MA
1987-1992	Assistant Physician, the Medical Service, Massachusetts General Hospital, Boston, MA
1992-	Associate Physician, the Medical Service Massachusetts General Hospital, Boston, MA

Other Professional Positions and Major Visiting Appointments:

1998-	President, Occupational Health Initiatives, Inc.
1998-	President, Occupational Health Institute
1996-1998	Executive Director, Public Health Research Institute
1996-1998	Medical Director & Executive Vice President, Public Health Resource Group, Inc.
1992-1998	Medical Consultant to the Commissioner of the Massachusetts Department of Industrial Accidents on implementation of medical provisions of the Massachusetts Workers Compensation Reform Act of 1991
1989	Adjunct Faculty, Department of Work Environment, University of Massachusetts Lowell
1979	Visiting Lecturer, Harvard School of Public Health
1979-1981	Occupational Physician, Medical Staff, Oil, Chemical and Atomic Workers International Union
1975-1978	Primary Care Physician, MGH Chelsea Health Center
1974-1975	Primary Care Physician, Morrisania Neighborhood Family Care Center, Bronx, NY
1971-1972	Director, Family Planning Clinic, Wake County Health Department, Raleigh, NC

AWARDS and HONORS:

1966	Phi Beta Kappa
1970	Alpha Omega Alpha
2006	Cushing-Gavin Award, The Labor Guild, Archdiocese of Boston

SERVICE ASSIGNMENTS:

1990-1996	Director, Occupational and Environmental Medicine, Massachusetts General Hospital
1990-1993	Assistant Director, MGH Employees Health Service
1980-1990	Co-Director, Occupational Medicine, Massachusetts General Hospital

MAJOR COMMITTEE ASSIGNMENTS:

Harvard School of Public Health:

1980-1983, 1992-	Advisory Committee, Residency Training Program in Occupational Medicine

Hospital:

1989-1990	Subcommittee on Human Studies, Member, Massachusetts General Hospital
1991-1996	Pulmonary and Critical Care Fellowship Review Committee, Member, Massachusetts General Hospital

Regional:

2003-	Contractor to Massachusetts Department of Public Health to consult on development of an asthma education program for construction workers and train community health care professionals to recognize occupational asthma
2001-	Member, Multiple Chemical Sensitivity Advisory Group, Massachusetts Department of Public Health
2000-2001	Member, Institutional Review Board, New England Research Institute, (NERI)
1995-1998	Science Advisory Board, The Massachusetts Toxics Use Reduction Institute, Governor-Appointed Member, the Commonwealth of Massachusetts
1994-	Asthma Treatment Guidelines Subgroup, Health Care Services Board, Chair, Massachusetts Department of Industrial Accidents
1993-1994	Program Committee, Regional Conference on Ergonomics, Safety, and Health in Construction, Member, Massachusetts Construction Safety Congress

1992-1998	Health Care Services Board, Commonwealth of Massachusetts, Chair
1998-	Health Care Services Board, Commonwealth of Massachusetts, Member
1984-1988	Scientific Advisory Council, Center for Health Promotion and Disease Prevention, Massachusetts Department of Public Health, Member

National:

1994	Planning Committee, Hazardous Waste Surveillance Program, Member, National Institute of Occupational Safety and Health/US Department of Energy
1992-1993	Planning Committee, International Congress on the Health Effects of Hazardous Wastes, Member, National Institute Environmental Health Sciences/EPA
1992-1993	Scientific Peer Review Committee for Enhanced Medical Surveillance Program for Beryllium Workers, Member, US Department of Energy
1990	Program Committee, Conference "The Third Wave of Asbestos Disease: Exposure to Asbestos in Place. Public Health Control", Member, Mt. Sinai School of Medicine, New York, NY; Harvard Medical School
1989	Steering Committee, Workshop on Environmental and Occupational Asthma, Member, EPA Task Force on Environmental Cancer and Heart and Lung Disease
1980-1982	Mine Health Research Advisory Committee, Member, National Institute for Occupational Safety and Health

MAJOR ADMINISTRATIVE RESPONSIBILITIES:

1998-	President, Occupational Health Initiatives/Institute
1996-1998	Executive Director, Public Health Research Institute
1996-1998	Medical Director and Executive Vice President, Public Health Resource Group
1992- 2000	Principal Investigator - Research project on health and safety hazards for construction workers on Boston Central Artery/Harbor Tunnel construction project, Public Health Research Institute
1990-1994	Director, MGH Occupational Health Associates, Massachusetts General Hospital

PROFESSIONAL SOCIETY INVOLVEMENT:

1975-	American Public Health Association, Member
1978-	American College of Occupational and Environmental Medicine (ACOEM), Member
1979-	Society for Occupational and Environmental Health, Member, Governing Council, 1986-1989
1982-	Massachusetts Medical Society
1982-1983	Council on Occupational Health, National Association for Public Health Policy, Secretary

1982- American College of Preventive Medicine, Fellow
1983- New England Occupational Medicine Association, Member Board of Directors 1983-1984
1984- American Thoracic Society, Member Program Committee, 1989-1992
1984- International Commission on Occupational Health, Member
1990- Association of Occupational and Environmental Clinics (AOEC), Member
1992- Collegium Ramazzini
1998- Physicians for Social Responsibility, Distinguished Physician

EDITORIAL BOARDS:

1990- American Journal of Industrial Medicine
1995- Applied Occupational and Environmental Hygiene

PART II:

A. Report of Teaching

1. Local Contributions

a. Medical School Courses

- Elective tutorial field study program in occupational medicine with the Oil, Chemical and Atomic Workers International Union
  Organizer and Course Director
  Four to five Harvard medical students; postgraduate students, Harvard School of Public Health; medical residents, Harvard Teacing Hospitals
  - Curriculum in Occupational Medicine funded by the National Fund for Medical Education
  Developer and Codirector, lecturer
- 20 Medical and postgraduate occupational health students: Harvard Medical School, Harvard School of Public Health
- Introduction to Clinical Medicine
  Clinical preceptor; lecturer on Occupational History Taking
  100 Medical students, lecture; three students, clinical preceptorship
- Patient-Doctor III
  Tutor
  Six Medical students
- Pathophysiology, Respiratory
  Lecturer, occupational lung disease; 100 medical students

b. Graduate Medical Courses/Seminars/Invited Teaching Preparations

- Occupational and Environmental Lung Disease
  Lecturer, introductory lecture series for first year pulmonary fellows
  Six to eight postdoctoral pulmonary fellows, MGH/Partners

- MGH Medical Grand Rounds/Malignant Mesothelioma
- MGH Medical Grand Rounds/Occupational Asthma
- Lecturer; MGH medical staff, house officers, fellows
- MGH Women in the Workplace Conference
  Lecturer, Occupational Risk Factors for Women
  Female hospital workers, approximately 50 attendees
- MGH Pulmonary/Critical Care Grand Rounds
  Lecturer, Medical-Legal Aspects of Occupational Medicine
  Lecturer, Occupational Asthma
  Lecturer, Occupational Lung Disease
- MGH Allergy Associates
  Lecturer, Occupational Asthma
  Lecturer, Building-Associated Illness
- Spaulding Rehabilitation Hospital
- Medical Grand Rounds, lecturer - Occupational Medicine

c. Continuing Medical Education Courses

- Massachusetts General Hospital, Harvard Medical School, Harvard School of Public Health: CME Course on Current Concepts in Asbestos-Related Disease
- Harvard Medical School Department of Postgraduate Education on Pulmonary/Critical Care Medicine
  Lecturer, occupational and environmental lung disease
- American Lung Association of Greater Norfolk County
  Lecturer, Occupational Lung Disease: an Overview
- Harvard Medical School Department of Postgraduate Education on Human Teratogens
  Lecturer on associations with occupational and environmental exposures

d. Advisory and Supervisory Responsibilities in Clinical Setting

- Director of elective in Occupational/Environmental Medicine for MGH Allergy/Immunology fellowship program
- Attending on the Pulmonary Consult Service
  Two to four trainees: average of two postdoctoral pulmonary fellows, one medical student
- Supervision of postdoctoral pulmonary fellows in interpretation and signout of pulmonary function tests performed in the MGH Pulmonary Laboratories
  Two to four trainees
- Supervision of postdoctoral pulmonary fellows in ambulatory care setting for patients with occupational/environmental lung disease on an ad hoc basis
  Fifteen trainees

e. Leadership Roles

- Title: (See IID, A1) Courses in occupational/environmental medicine for Harvard

medical students and other postgraduate students and residents
Primary Responsibilities: Development and organization of course curricula, contacting and scheduling lecturers, and preparation and presentation of teaching materials

- Special Accomplishments: 1) introduction of this type of course material (i.e., occupational and environmental medicine) back into the Medical School curriculum; and 2) the organization of courses that provided the opportunity for both didactic, tutorial, and worksite experience for students, as well as introduction to medical-legal and political aspects of occupational medicine, aspects to which students would not have had access otherwise.
- Title: "Asbestos in Commercial Buildings"
  Primary Responsibilities: Conceptualized, organized and moderated an interdisciplinary day-long seminar at the MGH
  Special Accomplishments: Invited lecturers, prepared teaching materials and syllabus, and created forum for discussion among affected parties of the burgeoning public health issue of asbestos in buildings. Attendees included physicians, attorneys, and building owners, developers, and mortgage lenders.

2. Regional, National or International Contributions

a. Invited Presentations

-Speaker and participant. Global Asbestos Congress. Osasco - Sao Paulo, Brazil
- Invited testimony before the House Judiciary Committee of the United States Congress on the HR 1283, the "Fairness in Asbestos Compensation Act of 1999"
- Panelist, "Women's Health Care in the 21st Century", Annual Conference, National Association of Commissions for Women, Boston, MA
- Lecture, "Multiple Chemical Sensitivity": A Wake-Up Call for the Public Health Community
  New England Public Health Association
- Lecture, Multiple Chemical Sensitivity
  Massachusetts Bar Association Environmental Law Committee
- Lecture, Multiple Chemical Sensitivity: Case Studies
  Massachusetts Continuing Legal Education, Inc.
- Lecture, Building-Associated Illness
  Administrative Law Judges Continuing Education, Massachusetts Department of Industrial Accidents
- Medical Grand Rounds, Occupational and Environmental Medicine
  St. Vincent's Hospital, Worcester, MA
- Lecture series for medical house officers; lecture on Occupational Medicine
  New York University (Bellevue) Hospital, New York, NY
- Lecture, Occupational Asthma, Occupational Medicine Residents
  University Hospital, Boston University
- Lecture, Medical Aspects of Workers' Compensation in Massachusetts - Medical and nursing staff

U Mass Worcester Medical Center, Worcester, MA
- Panel discussant, Health Hazards of Asbestos and Other Fibers
The Societe Internationale de Chirurgie, Paris, France-31st Congress
- Lecture, "Environmental Exposures and Risk Management", Environmental Health Education Project for Physicians and Health Professionals, Holyoke, MA
Massachusetts Department of Public Health
- Invited faculty member and lecturer on "Pleural Plaques and Lung Function"
American College of Chest Physicians, 57th Annual Scientific Assembly,
San Francisco, CA

b. Professional Leadership Roles Related to Teaching

- EPA, Workshop on Environmental and Occupational Asthma, Task Force on Environmental Cancer and Heart and Lung Disease, Long Beach, CA to develop a teaching program and materials for primary care physicians nationwide
Member Planning Committee; lecturer on "Occupational and Environmental Asthma: Legal and Ethical Aspects of Patient Management"
-American Society for Testing and Materials (ASTM)
Medical Session Chair and lecturer at the ASTM Conference on Indoor Air Quality, Johnson State College, Johnson, VT. ASTM conferences are international conferences held every five years to discuss timely and health-related issues.
-Massachusetts Department of Industrial Accidents, Massachusetts Medical Society
Teaching effort has been the organization and presentation of teaching materials in the area of medical issues in workers' compensation reform, primarily in the area of medical treatment guidelines in workers' compensation in general and treatment guidelines for occupational asthma in particular.
Lectures in this area have included the following: "Workers' Compensation: A Guide for Physicians", "Medical Treatment and Utilization Review. Massachusetts Workers' Compensation in the 1990's: Problems, Procedures and Perspectives", and "Treatment Guidelines and Utilization Review in Workers' Compensation in Massachusetts". Audiences have included members and officers of the Massachusetts Medical Society, the Eastern Association of Workers' Compensation Boards and Commissions, and the Southern Association of Workers Compensation Administrators

c. Professional Leadership Activities

2004: NIOSH Scientific Workshop relating to B Reader Certification Program.
Invited participant
2007: NIOSH Asbestos White Paper entitled "Asbestos and Other Mineral Fibers: A Roadmap for Scientific Research"
Invited Peer Reviewer

B. Clinical Activities

1. Clinical Practice - Field: Occupational/environmental medicine; Areas of major focus: a) occupational asthma; b) airways disease associated with construction work; c) asbestos-related disease; d) chemical sensitivities; and e) building-associated illness. Site of practice: MGH Pulmonary Associates.
2. Time Commitments - 25% Patient care; 5% teaching; 20% administration; 40% consultation; 10 % research.
3. Patient load, complexity - 15% asbestos-related disease; 20% building-associated illness; 20% chemical sensitivities; 35% occupational asthma; and 10% other.
4. Clinical program development - MGH Occupational Health Associates was an attempt to bring together a multidisciplinary team to provide medical services in the area of occupational medicine. Presently Dr. Oliver has one of the largest medical practices in the New England area for patients with building-related illness and chemical sensitivities.

C. Scholarly Contributions-Research that Contributes to the Care of Patients

1. Current Research Projects
   - Research on asthma in heavy and highway construction workers.
   - Research on asbestos-related in public school custodians, a 12 year longitudinal follow-up study.

2. Research Funding Information
   - Current years covered October, 2002-March, 2003; funding source Center to Protect Workers' Rights/NIOSH; Principal Investigator; "Asthma in Heavy and Highway Construction Workers Exposed to Silica".
   - Current years covered 1999-2003; funding source Manville Property Damages Trust; Principal Investigator; "Asbestos-Related Disease in Public School Custodians: a Longitudinal Follow-Up Study".

PART III: BIBLIOGRAPHY

Original Reports

1. Suberman (AKA Oliver) LC, Suberman RI, Dalldorf FG, Gabriele OF. Radiographic visualization of coronary arteries in postmortem hearts: a simple technique. Am J Clin Pathol 1970; 53:254-257.
2. San Agustin, M, Goldfrank L, Matz R, Suberman (AKA Oliver) LC, Hamerman D, Bloom R, Pilter D. Reorganization of ambulatory health care in an urban municipal hospital. Arch Intern Med 1976; 136:1262-1266.
3. Stoeckle JD, Hardy HL, Oliver LC. Women with asbestosis in a medical clinic: Underreported women workers, delayed diagnosis and smoking. Women in Health 1982; 17:31-36.
4. Banister EW, Fadl S, Brown S, Sprince NL, Oliver LC, Smith T, et al. A health evaluation study of kraft pulp mill workers. Proceedings of the Human Factors

Society, 1982.
5. Oliver LC, Weber RP. Chest pain in rubber chemical workers exposed to carbon disulfide and methemoglobin formers. Br J Indust Med 1984; 41:296-304.
6. Oliver LC, Eisen EA, Greene RE, Sprince NL. Asbestos-related disease in railroad workers:a cross-sectional study. Am Rev Respir Dis 1985; 131:499-504.
7. Ginns LC, Ryu JH, Rogol PR, Sprince NL, Oliver LC, Larsson CJ. Natural killer cell activity in cigarette smokers and asbestos workers. Am Rev Respir Dis 1985; 131:831-834.
8. Eisen EA, Oliver LC, Christiani DC, Robins SM, Wegman DH. Effects of spirometry standards in studies of two occupational cohorts. Am Rev Respir Dis 1985; 132:120-124.
9. Sprince NL, Oliver LC, McLoud TC. Asbestos-related disease in plumbers and pipefitters employed in building construction. Journal of Occupational Medicine 1985; 27:771-775.
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